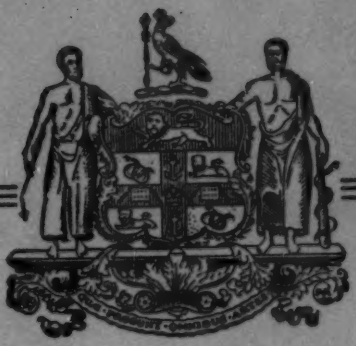

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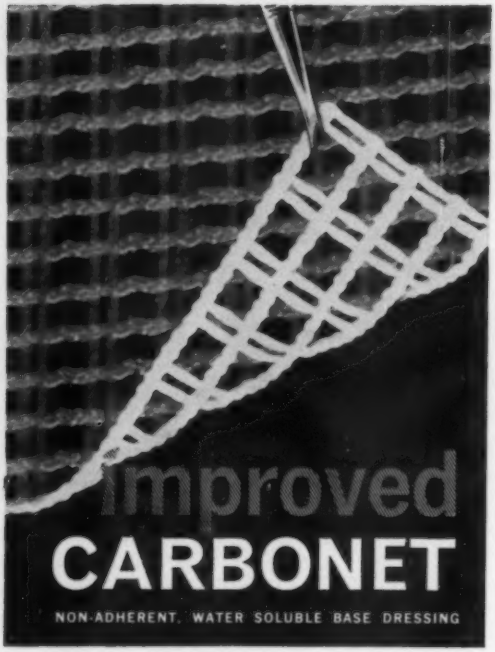

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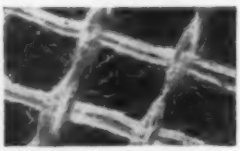

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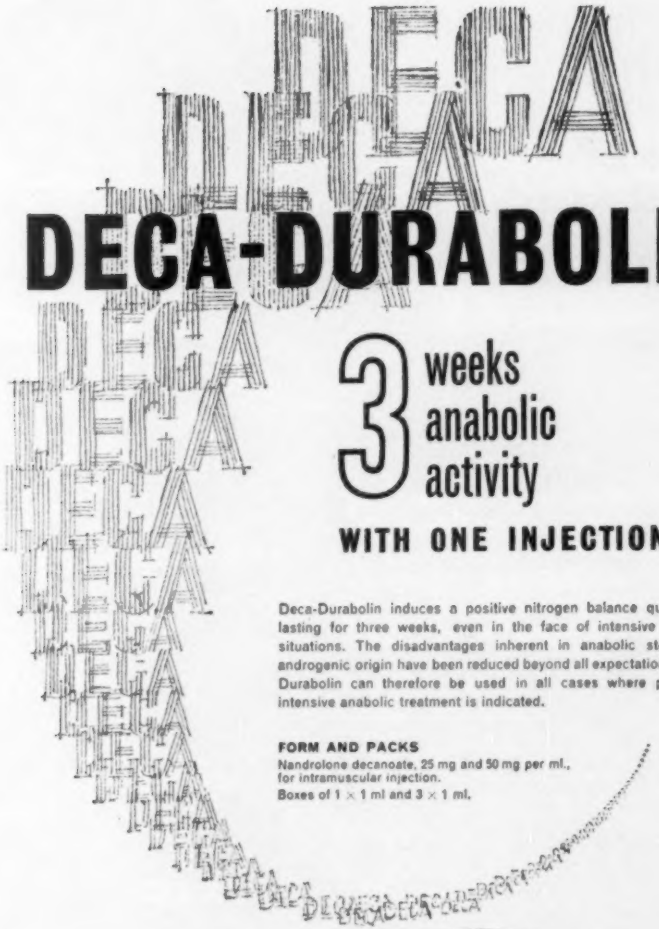

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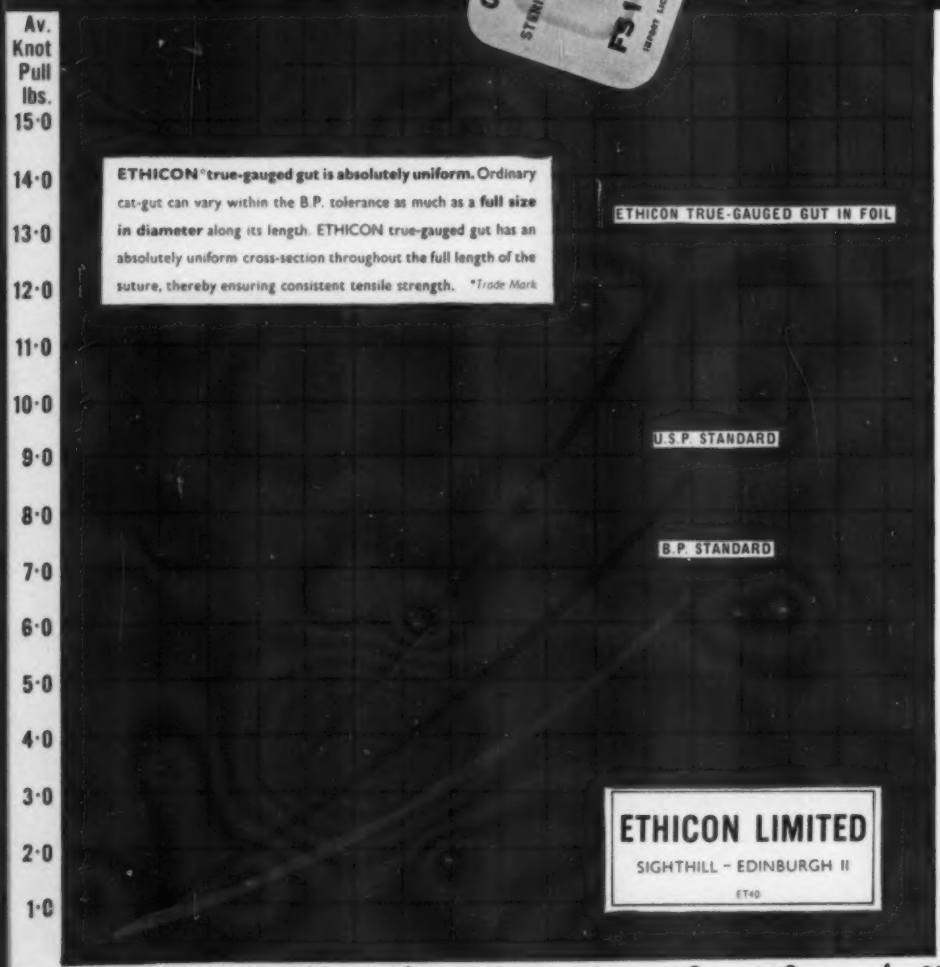

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ANNALS
OF THE
ROYAL COLLEGE OF SURGEONS OF ENGLAND

Editor :
SIR CECIL WAKELEY, BT., K.B.E., C.B.,
LL.D., M.Ch., D.Sc., F.R.C.S., F.R.S.E., F.F.R., F.D.S.R.C.S.

Volume 29 NOVEMBER 1961 No. 5

Published by
THE ROYAL COLLEGE OF SURGEONS OF ENGLAND
LINCOLN'S INN FIELDS LONDON, W.C.2

Annual Subscription - £2 post free
Single copies - - 3s. 6d. post free

ANNALS OF

THE ROYAL COLLEGE OF SURGEONS OF ENGLAND

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Telegrams : Collsurg, Holb, London

Cables : Collsurg, London, W.C.2 Telephone : Holborn 3474

THE FATE OF AUTOGENOUS TISSUE GRAFTS IN THE HEART

Hunterian Lecture delivered at the Royal College of Surgeons of England

on

11th April 1961

by

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INTRODUCTION

WITH THE RAPID development of cardiac surgery has come a need for materials that can be incorporated into the heart, both into its walls and into its chambers, to help in the correction of congenital and acquired

Fig. 1. The miraculous operation of Cosmas and Damian. The twin saints may be seen in the foreground having successfully amputated a cancerous leg from a white man and replaced it by the leg of a Moor, recently deceased.

abnormalities. This presentation is founded upon the belief that the patient's own tissues have pride of place as graft material in cardiac surgery, as much as in other branches of surgery.

The practice of tissue transplantation has its roots deep in surgical history and the reputation of the ancient Hindu surgeons' skill at skin grafting has come to us through the ages as a thing to marvel at. Myth and fable tell of less authentic grafting procedures, often undertaken with a bold disregard for the immunological problems associated with the transfer of portions of one person to another. Sixteen hundred and fifty years ago, the twin patron saints of surgery, Cosmas and Damian, were

responsible for a miraculous operation which must remain the envy of all those interested in organ or tissue transplantation at the present time (Fig. 1) (Singer and Singer, 1919).

John Hunter's interest in tissue transplantation is well known, and was closely bound up with his interest in the healing of wounds, and with broader concepts of tissue power. His practice of transplanting teeth was

Fig. 2. The head of a cock into the comb of which Hunter transplanted a spur. In its new position the spur grew to a length of 4 inches. (Pathological Series No. 532.1.)

founded upon painstaking animal experiment, and shows how much he appreciated the importance of a grafted tissue gaining a new blood supply in its new surroundings. In regard to his transplantation of the spurs of young cocks and hens (Figs. 2 and 3), he draws attention to the difficulty of translating experience with animal experiment into clinical practice; both observations are pertinent to this presentation.

HISTORY OF CARDIAC GRAFTS

Classification

In experimental and clinical cardiac surgery autogenous tissue grafts have been used in three ways.

First, for the artificial widening of the outflow portion of the right ventricle, pulmonary valve ring and pulmonary artery (pulmonary outflow tract).

Fig. 3. A section of the head of a cock and of a human canine tooth that Hunter transplanted, immediately after its extraction, into a puncture in the comb. (Pathological Series No. 540.1.)

Secondly, for the experimental production of mitral stenosis, for the control of valvar (chiefly mitral) insufficiency and for valve replacement.

Thirdly, for the closure of atrial and ventricular septal defects.

It can be appreciated that in the first group the graft is an intramural one, and that in the second and third groups it is intracavitary or a combination of the two.

For completeness this classification is extended to include the use of autogenous tissue grafts for the replacement of the great vessels, as the principles involved have bearing on the experimental work to be described.

INTRAMURAL GRAFTS

The earliest examples of tissue grafting in cardiac surgery are linked with the name of Theodore Tuffier (1857-1929). Tuffier was a pioneer in the field of thoracic surgery. He had a special interest in extrapleural pneumothorax and in 1891 performed what was probably the first successful resection for pulmonary tuberculosis, when he removed a part of the apex of the right lung. In 1913, the year that Doyen first tried to relieve

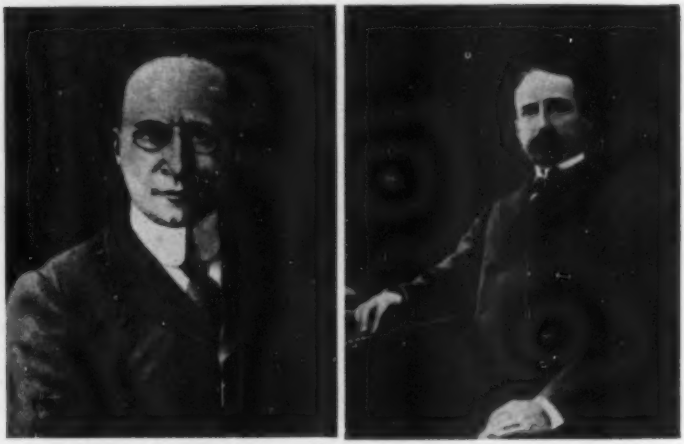

Fig. 4. Théodore Tuffier (right) and Alexis Carrel.

pulmonary stenosis with the knife, Tuffier made an attempt at aortic valvotomy, and in the same year was admitted an Honorary Fellow of the Royal College of Surgeons. In 1914, together with Alexis Carrel (Fig. 4), he wrote a paper entitled " Patching and Section of the Pulmonary Orifice of the Heart". In this paper, the authors described a series of experiments in eight dogs in which rectangular (2.5 × 2.5 cm.) patches of cold-preserved homologous vena cava were sutured as onlay grafts onto the outside of the right ventricle and pulmonary artery. The grafts were sutured in such a way that when a cut was made beneath the graft, across the valve, the edges could spring apart for a distance of 1 cm. In this way, they hoped to increase the circumference of the pulmonary valve orifice. One of their dogs died of ventricular fibrillation and another of purulent pericarditis, but they were satisfied with the result in their last four

experiments, and in one instance they were able to hear a pulmonary diastolic murmur. Although there is no description of the late results, and no record of this technique having been applied to humans, these experiments deserve respect and acclaim.

Thirty-six years later, Hufnagel (1950) made a similar series of animal experiments using onlay grafts of homologous aorta and vena cava, and also of autogenous pericardium. The principle of the experiments was identical with that of Tuffier and Carrel, the only refinement being the use of a wire pull-out suture to make the cut under the graft.

Kirklin (1953) described an operation for the relief of infundibular stenosis which made use of the cheese-wire technique without the overlying graft; and in 1958 from Budapest (Temesvari, 1958) came a report of punch resection of an infundibular stenosis beneath an onlay graft of autogenous skin. This first clinical application of the onlay graft technique, which followed animal experiment, was successful.

Lepley and others (1959), when investigating the fate of pedicled pericardial grafts in various situations in the heart, found that such a graft, when inserted between the edges of a linear right ventriculotomy, became converted into a contracted fibrous scar.

Also in 1959, the fate of a portion of urinary bladder was investigated when transposed to the outflow portion of the right ventricle as a free graft. Although survival of some of the smooth muscle was observed, and the transitional epithelium fared well in its novel surroundings, graft contraction was again noted (Daniel *et al.*, 1959).

After animal experiment, Gross (1961) has successfully applied autogenous pericardium to clinical use for the artificial enlargement of the pulmonary outflow tract in the treatment of Fallot's tetralogy.

INTRACAVITARY OR TRANSCHAMBER GRAFTS

Experimental valve (mitral) stenosis

In 1930, Professor Wilson of Aberdeen, then at Edinburgh, reported studies in experimental mitral obstruction which involved the introduction of various autogenous tissues into the cavity of the left ventricle. He found that fascia lata produced massive clotting with fatal results, and noted that tendon with its synovial covering was free from this complication. He used pericardium, and observed its gradual transformation into a tough inelastic cord when rolled up and used as a transventricular sling.

The control of valve incompetence

For many years it was hoped that mitral insufficiency could be cured by the fashioning of a loose sling, suspended across the cavity of the left ventricle, which could be swept upwards to plug the mitral orifice in ventricular systole.

The transventricular sling was made from a number of different tissues —vein (Murray *et al.*, 1938); inverted vein covering tendon (Murray, 1950a and 1950b), and pericardium as a rolled pedicle graft (Bailey *et al.*, 1951). Moore and Shumacker (1953) made a critical study of the fate of a number of autogenous tissues when transposed to the heart as a lax transventricular sling. They came to the conclusion that artery, vein, tendon, pericardium and rectus-fascia with a covering of peritoneum were all useless for the control of valve insufficiency by the " flutter tamponade " principle. All the tissues they tested became grossly fibrotic and contracted in a relatively short space of time, the final result being described as a fibrotic, rigid and amorphous ghost of the transplanted tissue. Similar conclusions had been reached by Glover and others (1952) and by Henderson and Law (1953) in studies confined to the fate of intracardiac tubed pericardial grafts.

In 1952, Logan and Turner reported the clinical use of strips of pericardium introduced by a closed method beneath the incompetent mitral valve, and the following year Bolton and others (1953) described ingenious ways in which inverted veins or pericardial strips could be used to suture the incompetent mitral commissure.

Glenn and others (1954), following the observation that mitral regurgitation could often be controlled by the exploring finger in the left atrium, fashioned autogenous inverted vein grafts containing the mobilized internal mammary vessels. These grafts were inserted from left atrium to left ventricle through the mitral valve in the hope that they would come to lie in the incompetent part of the valve orifice.

Valve replacement

Templeton and Gibbon (1949) made the first attempt, in experimental animals, at anatomical replacement of a resected valve cusp. Using autogenous grafts of vein and pericardium, and circulatory arrest at normal temperatures, they resected and replaced a tricuspid valve leaflet in 19 animals. Although the early results were encouraging, and pericardium seemed to be faring better than vein, the late results were disappointing.

Litwak and others (1952) invented an ingenious way of excising and replacing pulmonary and aortic valve cusps in the experimental laboratory. They proved that homograft valve cusps failed to stand the test of time, whereas a valve prosthesis made partly of autogenous pericardium and partly of aortic homograft gave very much more satisfactory physiological results for periods of up to four and a half months, and proved more satisfactory when examined histologically.

Bakst and others (1958) were satisfied with their carefully fashioned pericardial grafts six and eight months after they had been put in by a closed method to replace a partially resected mitral valve leaflet.

Lower and others (1960) have succeeded in resecting the entire pulmonary valve and transposing it to the descending aorta as a free graft. An autogenous valve transposed in this way, or replaced in its normal position, will survive, whereas free whole-valve homografts degenerate.

Closure of septal defects

In spite of its bad reputation for clot formation, fascia lata was chosen by Murray (1948) for the first attempts at closure of ventricular septal defects in man. Strips of fascia lata were passed blindly through the defects, the patients were heparinized from the second or third post-operative day and there was no evidence of embolism. There was, however, no good evidence that any of the defects were closed, occlusion depending upon the graft being sufficiently bulky for it to plug the hole as it was drawn through.

There followed an era when many workers devoted much time, energy and guile to the experimental creation and closure of atrial and ventricular septal defects. Those who used autogenous tissue grafts, chiefly of pericardium, were Kiriluk and others (1951); Shumacker, Moore and King (1953); Shumacker (1953); Bailey and his colleagues (1952) and Bahnson and Baker (1953). The development of the atrial well by Gross in 1952 made accurate placing of the grafts possible and he took full advantage of this to study the fate of autogenous pericardium, inverted vein and the tip of the right atrial appendage, when used as free grafts to close experimentally made atrial septal defects (Gross *et al.*, 1952, 1953). Both Gross and Bahnson found that pericardium was difficult to handle, and the difficulty of feeling soft tissue grafts using the well technique was a major reason for their being abandoned in favour of more rigid plastic substances. Donald, Kirklin and others (1953), making use of the atrial well, assayed various methods for the closure of atrial septal defects, which included the use of ivalon sponge plugs covered with pericardium. They concluded that ivalon sponge, alone or covered with pericardium, was preferable to direct suture or the use of polythene sheet, but did not make any recommendation for using pericardium in this way.

Lepley and others (1959), making use of cardio-pulmonary by-pass, have shown that the natural history of pericardial grafts, when used to close acute ventricular septal defects in dogs, is that they become shrunken fibrous scars with a tendency to calcify. It is difficult to make ventricular septal defects in dogs that mimic the congenital defect found in man. Such results must, therefore, be accepted with reserve, although the behaviour of these septal grafts is consistent with the behaviour of pericardium generally when used inside the ventricles.

Brock (1961) has been using free grafts of autogenous pericardium for the closure of human ventricular septal defects since November 1959.

J. K. ROSS

AUTOGENOUS TISSUE GRAFTS AND GREAT VESSEL REPLACEMENT

Autogenous pericardium used as a free tubed graft has been proved a reliable substitute for thoracic aorta, preferably supported by a layer of fascia lata (Sako and Varco, 1952; Adler, 1955). Autogenous pericardial grafts have been used experimentally to replace the main pulmonary artery and its bifurcation (Sauvage *et al.*, 1960) and autogenous vein and pericardium were proved the most satisfactory in a comparative study of tissues used for vena caval replacement (Sauvage and Gross, 1960).

To summarize the development of tissue transplantation in cardiac surgery, it may be said that the earliest exploit was to apply a graft to the heart for the relief of stenosis—in this case of the pulmonary valve. This technique was later revived, and in due course applied to human beings with success, for the artificial enlargement of the pulmonary outflow tract, both before and after the advent of the heart-lung machine.

As soon as the surgical treatment of mitral stenosis became commonplace, surgeons had to face the problem of mitral incompetence. This induced a lively interest in the control of valvar insufficiency by some form of intracardiac graft. The historical fact that this interest grew at a time when it was not possible to operate upon the interior of the heart under direct vision meant that the grafting techniques were restricted, and possibly misapplied, in terms of the properties of the tissues used, although much useful information was gained. None of the ways in which autogenous grafts were used proved entirely satisfactory for the control of valve incompetence. Coincidently with the coming of unhurried open heart surgery, synthetic substances were introduced which were more attractive to the surgeon as prosthetic material than the patient's own tissues. With the poor reputation of autogenous tissue grafts as checkers of valve incompetence, it was natural that synthetic valve prosthesis should be developed. The early results of some seem encouraging. It is suggested, however, that before completely abandoning them, autogenous tissue grafts are worthy of reappraisal in this context, taking advantage of cardio-pulmonary by-pass and profound hypothermia in the experimental laboratory.

Once it became established that most atrial septal defects could be satisfactorily closed by direct suture, interest in the use of tissue grafts for this purpose waned, though when properly used they had never been found wanting in the closure of experimental atrial septal defects. Although subject to some shrinkage, functionally and histologically they had proved entirely satisfactory. However, the ease of handling of synthetic prostheses, together with the impressive way in which the insertion of foreign material is tolerated by the heart, had already ensured the popularity of such methods.

The experimental work now to be described is a study of the fate of two tissues, namely tendon and pericardium, when introduced into the heart as free autogenous grafts. Tendon was inserted as a transchamber or intracavitary graft, and pericardium as an intramural graft.

TENDON GRAFTS

Experimental method

This study was carried out in 11 mongrel dogs weighing between 9.9 and 20 kg.

The tendon chosen for transplantation was that of the extensor digiti tertii et quarti muscle because of its calibre and length, and because its removal did not cripple the animal. This tendon was removed from the right forelimb, from its musculo-tendinous junction to the extensor retinaculum. In six instances the paratenon was carefully removed from the graft and in the remaining five it was left intact. The free segment of tendon was fixed at one end to a blunt probe and then kept immersed in normal saline.

The right side of the chest was then opened at the upper border of the fifth rib. The pericardium was incised and a stay suture placed through the apex of the left ventricle in the manner described by Elliott Cutler enabled the heart to be lifted out of the pericardium. With the heart thus up-ended, the probe carrying the tendon was passed through the heart from right to left across both ventricles. On two occasions, a rather longer graft was used and passed back again from left to right, leaving a loop on the outside of the left ventricle and producing a " double-barrelled " preparation.

Fixation of the graft. In three animals, the tendon was trimmed flush with the ventricular wall and fixed by two or three sutures which included the margin of the tendon and adjacent heart muscle. In five instances the excess tendon at the right ventricular end was buried in the myocardium, and in three both ends were embedded, all by the simple process of cutting the myocardium to make a trough for the tendon, which was then laid in the groove and oversewn. On five occasions, in a further attempt to improve the potential blood supply of the graft, the pericardium was sutured carefully over and round the entry wound in the right ventricle. In all, the tendon was fixed under slight but definite tension, sufficient in two to produce dimpling of the right ventricular wall. Care was taken not to twist the graft. There was very little blood loss during these procedures and, although there were transient arrhythmias, there was no incidence of heart block. There was no operative mortality, nor was there evidence that the heart action was embarrassed by the grafts.

Results

Fate of the animals. Of the 11 animals, five were kept for three months before ending the experiment and examining the grafts, and two were examined at 14 and 30 days respectively.

Of the remaining four, one was killed in a fight at 40 days, two died for no obvious reason at 14 and 47 days and one died in an emaciated con-

NO.	DAYS	GROSS APPEARANCE R. L.	TENDON BURIED R.	TENDON BURIED L.	PARATENON REMOVED	PERICARD. FIXATION
1	14		o	o	o	o
2	14		+	+	o	+
3	30		+	o	+	+
4	40		o	o	o	o
5	47		+	+	o	o
6	55		+	+	o	+

Table I. Tendon graft results. The grafts and the right and left ventricles are diagrammatically shown in the third column.

dition at 55 days. This last animal was the only one in which infection occurred, and its death may have been related to this; there was, however, no evidence of bacterial endocarditis.

Fate of grafts

Naked-eye appearances. The gross appearances and fate of the grafts is summarized in Tables I and II. In three of the 11, the tendon had partly or completely disappeared. Loss of the graft in one of these was plainly due to infection and an abscess was found in the left ventricular wall where the tendon had passed through. In one of the double-barrelled preparations the " return " limb of the graft was found ruptured in the left

ventricle at 47 days, with corresponding absence of the rest of it from the right ventricle. The third showed disappearance of the left ventricular portion but survival of the part in the right ventricle, and both these latter failures are presumed to be due to avascular necrosis of the graft.

Mottled discoloration was noted in three grafts: in two examined at two weeks and in one after 40 days. Small nodules of thrombus were found on the left ventricular part of two grafts.

From the second week onwards, the tendons, which had been typical flat extensor tendons when they were put in, had become round in cross-

NO.	DAYS	GROSS APPEARANCE	TENDON BURIED		PARATENON REMOVED	PERICARD. FIXATION
		R. L.	R.	L.		
7	96		+	o	+	o
8	98		+	o	+	+
9	104		+	o	+	+
10	110		o	o	+	o
11	119		o	o	+	o

Table II. Tendon graft results. This table shows the results in the long-term (three-month) survivors.

section, and wherever the graft had crossed an endocardial surface the two had blended smoothly together. Also, the grafts had become firmly fixed to the interventricular septum.

Those in which the whole graft had survived after three months showed loss of flexibility, but they were not completely rigid and macroscopically their appearance was encouraging (Fig. 5). There was no evidence of shortening or elongation of any of the grafts.

Microscopic appearances. The tendon grafts were all sectioned longitudinally and sections of the adjacent ventricular wall and septum were also made. These showed that, for the first month, the grafts could remain viable, and that any platelet thrombus which collected on their surfaces became flattened and covered by endothelium. From that time onwards,

however, progressive degeneration of the grafts took place, so that by the end of three months the tendon was being replaced by structureless basophilic tissue with focal calcification (Fig. 6). Islands of recognizable tendon remained, however, for a surprising length of time (Fig. 7).

The early naked-eye observation of mottling was associated with the histological finding of focal haemorrhage into the graft; it is not known whether all the longer survivors had at some time shown this change or whether this was a prelude to early disruption of the graft.

The surface of the tendon itself was covered by a peripheral zone of cellular tissue which at first was quite broad, but which became pro-

Fig. 5. The left ventricle opened to show a tendon graft three months after introduction.

gressively flattened and less cellular with the passage of time. This zone was broader and had attracted more platelet thrombus in those instances where the paratenon had not been removed. It was also in the marginal zone that the earliest signs of calcification appeared, early in the second month, the tendon itself only being affected later.

Clear evidence of vascularization of the graft was found in the 30-day preparation, but blood vessels could not be seen in the older ones.

Acute inflammatory changes were found in the myocardium close to the graft on two occasions, and in one the microscopic appearances confirmed

the naked-eye diagnosis of an intramural abscess in the left ventricle. The remainder showed little inflammatory cell infiltration except in the region of suture material. In all, the endothelial lining of the ventricle had become continuous with that covering the graft.

Comment

This investigation has shown that survival of free tendon grafts within the ventricular cavities is unpredictable, and that serious degenerative changes occur within the space of three months.

Fig. 6. Microscopic appearance of a tendon graft at 47 days (×40). Focal calcification occurring in tissue resembling cartilage.

Peacock (1957) has shown that tendon is a tissue with measurable metabolic requirements and that its survival as a free graft depends upon direct contact with the blood vessels of the host tissue. Further, he has shown that such vascular contact must be made at either end of the graft and at some intermediate point as well if survival of the graft is to take place. These requirements were fulfilled in my experiments, at least in theory, in that the grafts were given the opportunity of gaining a blood supply both from the ventricular walls and the interventricular septum. That the grafts survived at all, together with the fact that blood vessels could be identified within the tendon one month after transplantation, is taken as evidence that vascularization was initially successful. The degenerative changes must be related to the eventual failure of blood

supply, which, in turn, may be nothing more than an expression of a normal reaction to abnormal stress. This theory is upheld by the fact that disruption or disappearance of two of the grafts took place only in the high-pressure left ventricle and not in the right. Histologically, however, there was little or no difference in appearance between the parts of the grafts in the right and left ventricles; but in one there was good evidence of progressive degenerative change along the length of the graft the further away it got from the ventricular septum.

There was no evidence that the mode of fixation of the graft, or the local attachment of pericardium at the graft entry wound, made any difference to the eventual fate of the tendon.

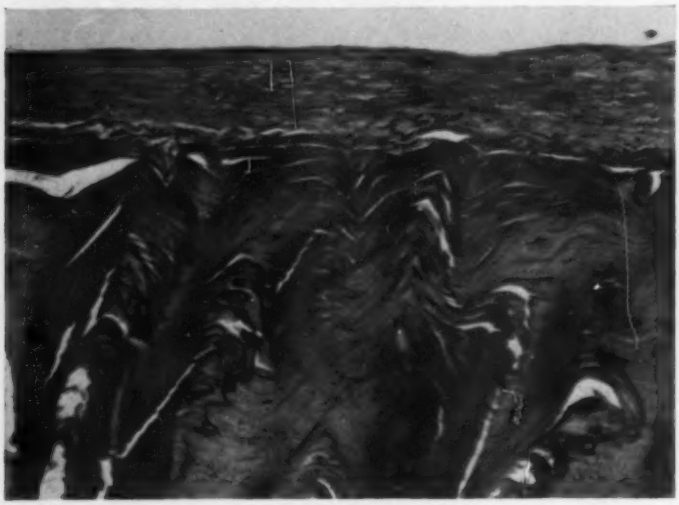

Fig. 7. Photomicrograph of a tendon graft at three months (×40). Part of an island of recognizable tendon, and the thinned peripheral zone are shown.

The removal of paratenon may possibly have helped early graft survival, but did not affect the ultimate outcome.

Thrombus formation never occurred to a serious degree.

PERICARDIAL GRAFTS

Experimental method

In 30 adult mongrel dogs of average size, an operation was performed by means of which a free pericardial graft was substituted for a substantial portion of the anterior wall of the pulmonary outflow tract.

The animals were divided into two groups of 15 in which the graft was either left unsupported or was reinforced by a second layer of autogenous tissue. In the second group, the reinforcing layer was of fascia lata in 13 instances and of pericardium, as a pedicled flap, in two.

A further subdivision was made in that eight grafts were restricted to the right ventricular wall in the subvalvar position, and the remaining 22 were made to extend across the pulmonary valve ring, and thus to replace part of the wall of the main pulmonary artery as well (Table III).

The details of the experimental technique are illustrated in Figure 8. Hypothermia by surface cooling and circulatory arrest by inflow occlusion gave adequate conditions for the experiment. Ventricular fibrillation complicated 10 experiments, but was successfully reverted in each case by

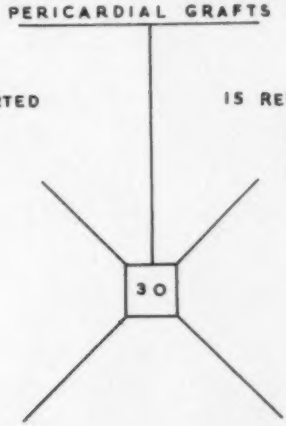

Table III. Pericardial grafts. To show the subdivision of the experimental method in 30 animals.

conventional methods. The size of the excised portion of tissue varied slightly, but an average of 4.1 sq. cm. was removed in each instance: part of the pulmonary valve ring and at least one pulmonary valve cusp were removed whenever the excision extended into the pulmonary artery. It proved to be important to make the pulmonary artery end of the graft square rather than pointed to avoid narrowing of the pulmonary artery at the apex of the patch. A similar technique has since been described by Sauvage and others (1960).

Before deciding upon the above technique for these experiments, trial had been made of linear ventriculotomy beneath an onlay graft in the manner of Tuffier and Carrel. It was found, however, that although the space under the graft filled with blood and made the graft itself bulge, the cut edges of the myocardium quickly came together again underneath.

Also, tangential clamping of the right ventricle and pulmonary artery, sufficient to allow resection and replacement of a large enough portion of outflow tract wall, produced prohibitive obstruction to right ventricular emptying.

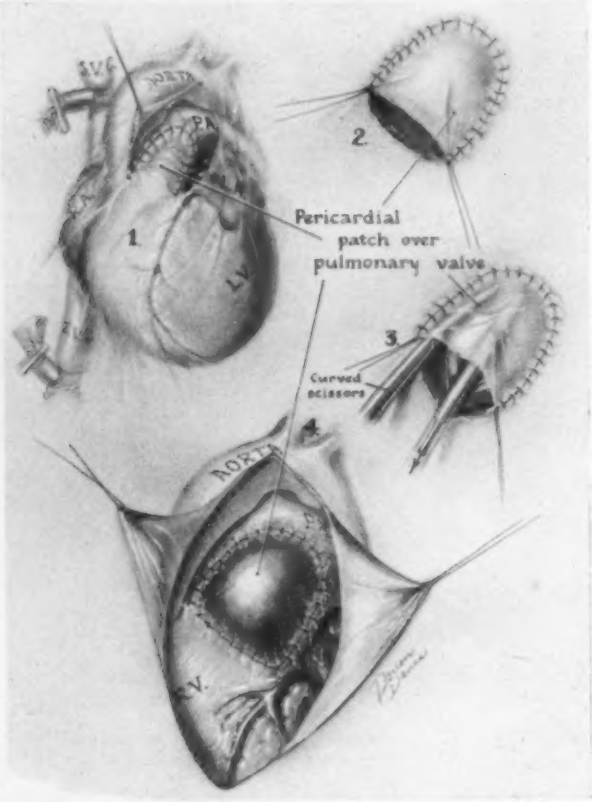

Fig. 8. The technique of replacement of part of the pulmonary outflow tract by a pericardial graft. The pericardium is carefully incised and sutured taut over the area to be excised (1). Removal of the required amount of pulmonary outflow tract wall from beneath the graft (2 and 3) is followed by completion of the suture line (4) and restoration of the circulation.

Single animals were sacrificed at periods of two weeks, one month, three months and five months after operation, and the 13 long-term survivors at six months. Autopsies were made on all those dying unexpectedly. Whenever an animal was to be deliberately put down, a second formal thoracotomy was made with full exposure and examination

of the graft in the beating heart. On two occasions, this live examination was supplemented by high-speed cinematography. At intervals, animals were selected at random for chest radiographs. These were found difficult to interpret; they gave little valuable information in the light of subsequent autopsy findings, and their use in every animal was therefore not pursued. More valuable information was got by the use of cine-angiocardiography, which was undertaken in three animals with transvalvar grafts and known pulmonary regurgitation. In each case, injection of medium into the pulmonary artery was followed by outlining of the graft area as the dye was swept back into the right ventricle in diastole.

Histological examination of all the grafts was made.

Early Results

Early fatalities. There were ten post-operative deaths within the first month, and three deaths from distemper between one and two months after operation.

All ten of the early post-operative deaths were due to errors in experimental technique or after-care. There was a decline in the death rate as the series progressed and there was no unexpected death more than two months following operation; this does not suggest that there was any factor involved which caused natural progression to death.

Two animals died during the first 24 hours after operation, one of atelectasis and the other from occlusion of the pulmonary artery by a large thrombus, fixed to the cut edge of the myocardium and propagated beneath the graft. A third died with a massive pleural effusion on the sixth day.

Haemothorax. Bleeding caused the death of four animals between the sixth and eighth post-operative day. In one of these, the edge of the graft had burst at a point where pericardial fat and not pericardium had been included in the suture line. Following this fatality, great care was taken to remove all fat from the graft. In two instances no source for the bleeding could be found, and the fourth was due to secondary haemorrhage in association with an infected fascia lata reinforcement.

Empyema. Three deaths due to empyema took place between the twelfth and twenty-fourth day after operation. In none of these was there evidence of extension of suppuration to the pericardial graft or evidence of septic pulmonary emboli.

Late results (three-to-six months; 15 animals)

Dilatation of the graft. The animal examined at three months showed definite systolic bulging of the graft area and this suggested that aneurysmal changes could be forecast in those to be inspected later. However, this proved to be an isolated finding and dilatation of the graft was not found in the remaining animals. This was confirmed by the findings on cine-

angiocardiography (Fig. 9 (*a*) and (*b*)) (and on chest radiographs) which showed no evidence of aneurysmal bulge of the grafts in the closed chest. High-speed ciné film confirmed with precision the absence of graft dilatation at second thoracotomy.

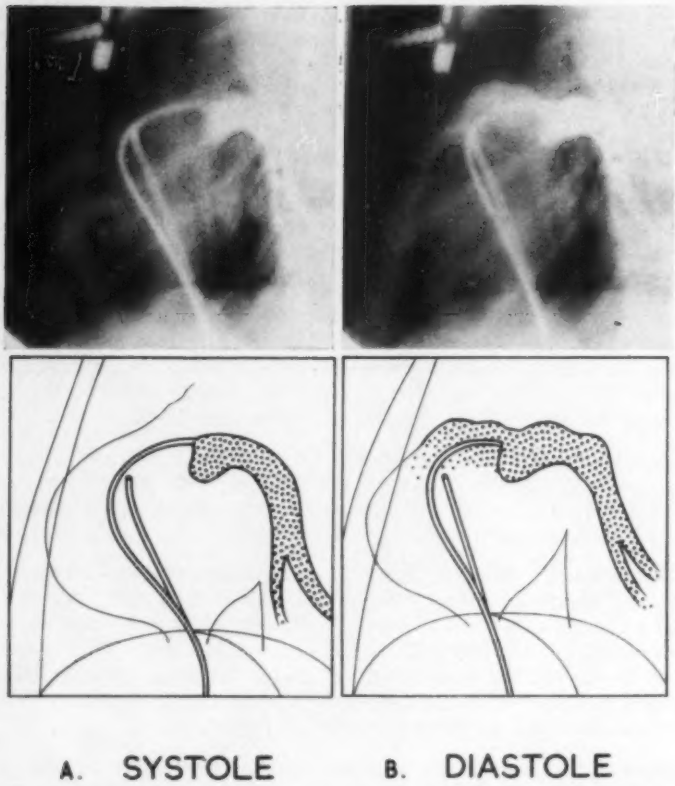

Fig. 9. (*a*) Cine-angiocardiogram—systole. An injection of dye has been made into the pulmonary artery, and a second cardiac catheter lies with its tip in the right ventricle for pressure measurements. Lateral projection. (*b*) Diastole. Dye has been swept back into the right ventricle due to the presence of free pulmonary regurgitation. The grafted area is outlined and no significant bulge is shown. Analysis of the films failed to show any dilatation of the grafts in systole either.

Graft contracture. With one exception, all the grafts which did not extend across the pulmonary valve ring showed gross contracture (Fig. 10). All that remained was a puckered fibrous scar, often with calcification and, in one instance, with the histological appearances of bone. The one

surprising exception was the graft showing dilatation at three months, which had been placed in the subvalvar position.

In sharp contrast to this observation, the 10 long-term transvalvar grafts (Fig. 11) included only one showing any evidence of contracture. In this instance, contracture had occurred to a much lesser degree than that shown by the subvalvar grafts, and it is not known whether the pericardium or the overlying fascia lata support was responsible for the shrinkage.

Fig. 10. The right ventricle and main pulmonary artery opened to show the typical appearance of a subvalvar pericardial graft after six months. It has become converted into a shrunken fibrous scar.

All the grafts were covered by dense vascular adhesions to the lungs and mediastinal connective tissues.

Thrombus formation. In none of the long-term survivors was thrombus found on the endocardial surface of the grafts. In the series as a whole, thrombus was found beneath the graft in seven animals. In four it was very thin and tightly fixed to the graft. In two instances of fatal haemothorax larger thrombi were found, while in one, previously mentioned, it was considered to be the cause of early post-operative death. Examination of the lungs in the longer survivors did not show gross or microscopic evidence of past pulmonary emboli.

Unsupported and reinforced grafts. The group in which the graft was left unsupported fared better than that in which fascial or pericardial reinforcement was added. Almost twice the number of unexpected deaths occurred in the latter group, but this was principally due to an increased incidence of infection. The incidence of fatal haemothorax was the same in both groups. Since none of the grafts disrupted centrally or became aneurysmal, it appears that a single layer of pericardium is sufficient to withstand the stress of normal right ventricular pressures and that the addition of a reinforcing layer is unnecessary.

Fig. 11. The right ventricle and main pulmonary artery opened to show a transvalvar graft after six months. It is the same size and shape as when it was put in, and showed no dilatation when examined *in vivo*. Only one cusp of the pulmonary valve remains intact. (Compare Fig. 10.)

Histological appearances. The subvalvar grafts, used to replace a portion of the right ventricular wall only, became converted into contracted fibrous scars with a tendency to calcify, the histological appearances merely confirming the naked-eye observations. In one instance, there were two areas in which bone had developed in the scar.

The transvalvar grafts, on the other hand, retained their essential histological characteristics, showing robust collagen fibrils with the van Gieson stain (Fig. 12). Intact endothelium on the ventricular surface of the graft, together with absence of thrombus, could be demonstrated in all the long-term preparations. At the margins, the graft was found to have merged

satisfactorily with the myocardium, with minimal reaction, and a vascular adventitial layer of varying thickness was found on the outer surface of the pericardial patch.

Comment

The most important fact established by this study is that a free autogenous pericardial graft is able to survive and withstand repetitive stress in its new environment over a long period of time. In none of the 30 experimental animals was there evidence of rejection of the graft.

The high overall mortality has been shown to be due to technical errors rather than to failure of the grafts themselves.

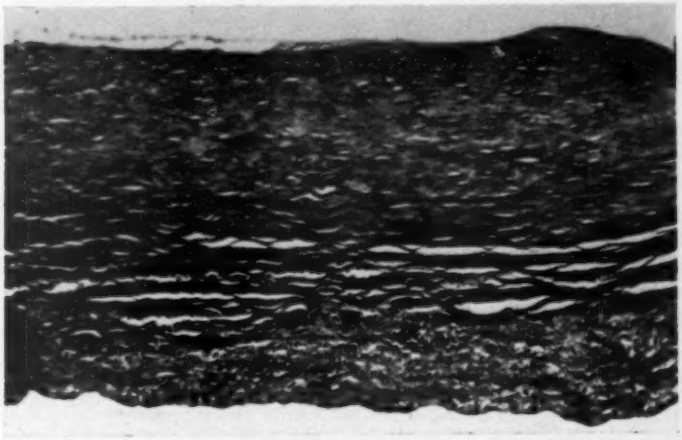

Fig. 12. Photomicrograph (×28) of free, unsupported pericardial graft after six months. The endocardial (top) and vascular adventitial layers are well seen, and darkly stained collagen fibres (van Gieson preparation).

The evidence regarding thrombus formation suggests that clot formed on the raw exposed surface of the cut myocardium and not on the pericardial graft itself. This complication was therefore related to an unavoidable weakness in experimental technique rather than to an inherent property of the pericardial graft.

The use of fascia lata to reinforce the pericardial patch was suggested by the work of Sako and Varco (1952), who showed the ability of fascia lata to prevent dilatation of autogenous tubed pericardial grafts when these were used to replace segments of thoracic aorta. Comparison of the unsupported and reinforced grafts in the present series has shown that the addition of a second layer contributes nothing to the end-result. It is not known whether suitable reinforcement would be necessary if the right ventricular pressure were abnormally high.

The only common factor among the grafts which resisted contracture was the presence of free pulmonary regurgitation. In only one animal with an intact pulmonary valve did contracture of the graft not take place. It seems, therefore, that pulmonary valve insufficiency, possibly by maintaining stretch at the graft site, helps the graft to keep its original size and shape.

None of the animals whose pulmonary valves had been partly resected showed evidence of right ventricular embarrassment.

DISCUSSION

What are the essential properties of a tissue to be transposed to the heart?

First it should be capable of retaining its normal structural characteristics and of fulfilling its designed function for long periods of time. Secondly it should not by its presence embarrass the action of the heart; and thirdly it should not provoke the formation of thrombus. Secondary changes within the tissue graft following upon its change in environment are permissible, provided the functional result is not impaired. Thus, for example, if pericardial grafts used for the closure of ventricular septal defects are found to calcify, this secondary change is immaterial provided the closure remains intact.

There are few human tissues which have the necessary properties for survival and continued function when transposed to the heart as free grafts. High tensile strength and an ability to withstand repetitive stress during the period while a fresh blood supply is being gained are essential. Further, it is important that the natural properties and function of the grafted tissue be borne in mind. It was for this reason that the tendon grafts described were fixed so that they were taut, ensuring mainly longitudinal stress for which this tissue is specifically designed. The hope that free tendon grafts might be of value for the replacement of ruptured or deformed chordae tendinae has not been upheld.

The natural properties of pericardium have been ignored frequently in the past when this tissue has been grafted into the heart. Normal pericardium is well known for its ability to withstand an acute expanding force and it is structurally adapted to resist stretch. It is hardly surprising, therefore, that, when rolled up into a cord and suspended across a ventricular cavity, it should retain neither its structure nor its desired flexibility. The success of the transvalvar pericardial grafts here described, and the failure of those placed in the subvalvar position, may be related to the degree of stretch at the graft site.

The natural history of free tissue grafts in the heart is closely bound up with the problems of their gaining a fresh blood supply. Nourishment for the graft may be obtained from the blood circulating in the chambers of the heart, but this is far from certain. Link-up of the intrinsic blood vessels of the graft with those of the coronary circulation takes time to accomplish, and has to take place, contrary to the accepted principles of rest and wound healing, in a state of constant movement. This may be why intracavitary, particularly intraventricular, grafts tend to die and calcify. Alternatively, tissue death and calcification in such grafts may be a late secondary change due to a delayed failure of vascular supply following abnormal stress. Intramural grafts, on the other hand, have an extra source of blood supply in the vascular adhesions to the lung and mediastinal connective tissues which form rapidly on their outer surfaces. This may be an important factor in their successful survival. For this reason, too, the interposition of a second reinforcing layer between the graft and its vascular surroundings may be a mistake.

The two tissues chosen as graft material in this study are composed largely of collagen—in tendon as a coarse, multiple-ply arrangement and in pericardium as a much finer laminar mesh. The problem of the biochemical changes occurring in such free collagen grafts in the heart has not been investigated here, beyond the retention or otherwise of the staining properties of the grafted material.

CLINICAL APPLICATION OF AUTOGENOUS TISSUE GRAFTS

I am greatly indebted to the following surgeons for letting me describe their personal experiences with the use of autogenous tissue grafts in the heart.

During 1959, Dr. Frank Gerbode of San Francisco used pericardial grafts for the artificial enlargement of the pulmonary outflow tract on seven occasions. All but one of these grafts were reinforced by an overlying patch of woven Dacron, and proved entirely satisfactory. In one instance the graft was reinforced by a second layer of pericardium as a pedicled flap. This graft showed some dilatation after three months (Gerbode, 1961).

Dr. Robert E. Gross of Boston has used free unsupported pericardial grafts for pulmonary outflow tract enlargement on a large number of occasions. He is entirely satisfied with the handling properties of pericardium and with the results of its use in this situation. With one possible exception there has been no incidence of graft dilatation in his series (Gross, 1961).

Sir Russell Brock has used free autogenous pericardial grafts for the closure of ventricular septal defects in a total of 35 cases. In over half (22) the graft constituted the entire closure and in the remainder (13) it was

used as reinforcement. Using his latest technique of a double-layered graft the results have been particularly satisfactory (Brock, 1961).

Finally, the use of autogenous pericardium for the closure of atrial septal defects of the ostium primum variety can be safely recommended.

SUMMARY

1. A review of the history of autogenous tissue grafting in experimental and clinical cardiac surgery has been given.

2. A series of experiments in which free tendon grafts were inserted across the cavities of both ventricles has been described. The fate of these grafts indicates that tendon is unsuitable material for an intracavitary graft.

3. A series of experiments in which free pericardial grafts were used to replace portions of the pulmonary outflow tract wall has been described. The results of these experiments show that such grafts, made to cross the pulmonary valve ring, survive and subserve their designed function.

4. The problems associated with free tissue grafts in the heart have been discussed and the successful clinical application of autogenous tissue grafts has been described.

ACKNOWLEDGMENTS

The experimental work described was carried out during 1959 in the surgical laboratory at San Francisco Stanford Hospital, and I wish to take this opportunity of thanking my chief, Dr. Frank Gerbode. The work on pericardial grafts was done together with Dr. George A. Harkins, now at the Children's Hospital in Boston. My thanks are also due to Dr. Abrams for the cine-angiocardiographic studies, to Dr. Harold March for the high-speed cinematography, and to the staff of the surgical laboratory for all their assistance. Finally I wish to thank the department of pathology, and Mr. A. Curd of the photographic department, at the Brompton Hospital for their considerable help.

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RECENT APPOINTMENTS OF FELLOWS AND MEMBERS

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THE EFFECT OF GASTRECTOMY ON PANCREATIC SECRETION IN MAN

Hunterian Lecture delivered at the Royal College of Surgeons
on
13th April 1961
by

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Consultant Surgeon, Frenchay Hospital, Bristol

INTRODUCTION

AT THE OUTSET, I would like to express my sincere gratitude to the President and Council for the honour of the office accorded to me and for the privilege of giving this lecture. The Hunterian tradition, embodying the concepts of experiment and the continued application of the basic sciences to surgery, has been emphasized in the policy of the College, and I trust that my lecture will serve to illustrate these concepts. Although the scope of surgical operations is determined largely by anatomical considerations, physiological criteria are assuming greater importance. The end results of surgical procedures must be physiologically acceptable. Consequently, we must be eternally critical of our results in order to achieve the most desirable benefit for patients. The results of gastrectomy have been reviewed in many centres, but it is my purpose to present a study of the effect of the operation on the function of a neighbouring organ, the pancreas.

Normally, the efflux of acid-chyme from the stomach results in the output of a corresponding volume of alkaline fluid into the duodenum, chiefly in the form of pancreatic secretion and bile. The factors involved in this response are hormonal (secretin and pancreozymin), nervous, and the constituents of food. Following gastrectomy and the subsequent anatomical reconstruction, new factors, such as reduced gastric secretion, increased emptying rate of the gastric remnant, alteration of pH, and the physical state of food leaving the gastric remnant, may modify the response occurring in the duodenum, especially if this part of the intestine is bypassed. It is reasonable to suspect that the hormonal mechanism for pancreatic secretion may not be as effective as in normal people. Further, since vagotomy is inherent in gastrectomy, any coincident denervation of the pancreas may alter its response to food after operation.

A review of literature

Experimental studies in dogs have shown that the pancreatic response is reduced after gastrectomy (Annis and Hallenbeck, 1952; Richman *et al.*, 1954). The early investigations of the problem in man, however, do not afford a clear picture of the effect of the operation. Fried and Stein (1923) observed compensatory hypersecretion by the pancreas, whilst Glaessner (1927) noted that the pancreatic output was reduced following

operation. Stern (1929) found normal enzyme output following gastrectomy. In all of these studies, however, segregation of gastric and duodenal secretion was not achieved, and enzyme estimations were unreliable.

Santy *et al.* (1939) believed that pancreatic insufficiency followed gastrectomy, and was due to reduced blood flow to the pancreas. They observed variations in lipase output after operation in contrast to Mikhlin and Levitskii (1955), who recorded increased lipase output. Unfortunately, lipase is notoriously unstable (Lagerlof, 1942), and is not a reliable index of pancreatic enzyme secretion.

Some investigators have used the secretin test to study pancreatic function after gastrectomy. MacLean *et al.* (1954) and Kelly *et al.* (1954) observed normal secretin responses following the Billroth I operation, but reduced response after the Polya operation in one-third of their patients. Dreiling (1957) also found evidence of pancreatic secretory defect with the same test.

The use of isotopic fat (Shingleton *et al.*, 1957; Baylin *et al.*, 1957; Ruffin *et al.*, 1958) has indicated that the absorption defect which follows gastrectomy is similar to that occurring in patients with pancreatic deficiency. This may be due either to reduced pancreatic output or to poor mixing of the meal and pancreatic enzymes.

Most valuable work has been done by Kiekens and Lundh (1957), and Lundh (1958). These authors carried out intubation studies on normal controls and on patients after gastrectomy. In the post-operative group, they found reduced concentrations of trypsin, and Lundh observed that the enzyme was occasionally absent. Only after food had left the proximal intestine did they record increase in enzyme concentration, which never attained normal levels after Polya operations, but occasionally did so following the Billroth I operation.

Warren (1954) stated that a reduction of pancreatic secretion could follow gastrectomy, but never with great frequency or severity. Dragstedt (1952) and MacLean *et al.* (1954) have expressed similar views. The opinion of the majority, however, is that pancreatic secretion does not have proper access to food following gastrectomy (Warren, 1954; Wells, 1955; Polak and Pontes, 1956; Kiekens and Lundh, 1957). Nevertheless, no clear picture is apparent. Several authors have indicated the need of an investigation of pancreatic secretion using food as a stimulus (Everson, 1952; Lundh, 1958; Rowlands, 1959), and this forms the basis of the present study. In addition, the role of the pancreas in relation to post-gastrectomy steatorrhoea has not been established, and an attempt will be made to correlate these.

T. J. BUTLER

PART I

PANCREATIC SECRETION BEFORE AND AFTER GASTRECTOMY

The work embodied in this lecture was carried out in Bristol during the past nine years. At the outset, it appeared that the study of pancreatic secretion after a Billroth I gastrectomy would be a reasonably straightforward procedure. The real problem was presented by the Polya operation. It will be readily appreciated that it is impossible to obtain samples of pancreatic secretion after this operation of such a type that they can be compared with pre-operative control samples. The difficulty was circumvented by doing all the intubation tests on patients before and after Billroth I operations, but in each case the meal was introduced either into the duodenum or into the jejunum directly by means of intubation. In this way, it was possible to compare the pancreatic response to food before and after gastric resection when the meal was put into the duodenum on the one hand, and into the jejunum directly on the other. The investigations were done on 87 patients altogether, being continued until 50 were completed. Each patient had four tests, two prior to operation to give controls, and two following operation. There were 37 failures, representing a success rate of 57.5 per cent. for the intubation technique. The results were grouped as follows:—

Series A. The pancreatic response to food entering the duodenum before operation.

Series B. The pancreatic response to food entering the jejunum before operation.

Series C. The pancreatic response to food entering the duodenum after gastrectomy.

Series D. The pancreatic response to food entering the jejunum after gastrectomy.

In each series, therefore, 50 results were available for analysis, and it is submitted that those in Series C indicate the pancreatic response occurring after a Billroth I operation, while those in Series D afford an approximate index of the response after a Polya operation.

A four-lumen tube was used throughout the investigation, and was modified to give separate access to the stomach or gastric remnant, the duodenum, and the jejunum (Butler, 1959). In the early stages of the investigation, balloons were used on the tube to occlude a section of the duodenum (Shingleton and Fawcett, 1951), but it was found that inflation of balloons in the duodenum caused ejection of the tube into the stomach or produced marked depression of pancreatic secretion. For these reasons, the use of balloons was discontinued.

The tube was passed under radiological control so that it occupied the position illustrated in Figure 1, the tip lying 5 to 7 cm. beyond the duodeno-jejunal flexure. The general technique of intubation is well

known, and it will suffice to say that the drill followed in these studies was similar to that of Lagerlof (1942), especially with reference to continuous suction, segregation of duodenal and gastric secretion, and the treatment of aspiration samples from the duodenum by ice-cooling and the addition of glycerine. The meal used in the tests consisted of 50 ml. of reconstituted whole milk powder with the addition of 10 G. of glucose and 3.5 G. of proteolysed liver. The composition, therefore, was 5.2 G. of protein, 1.7 G. of fat, and 12.34 G. of carbohydrate.

In the tests in Series A and C, two resting 10-minute samples of duodenal aspirate were collected first. 50 ml. of the meal were then introduced slowly into the duodenum over a period of four minutes—corresponding to the normal rate of gastric emptying. After two more minutes, the duo-

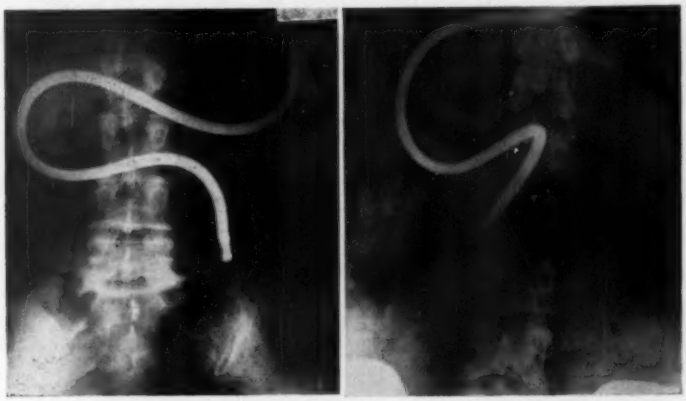

Fig. 1. X-ray picture to illustrate the position of the tube for the intubation tests. The tube is passed through the stomach (or gastric remnant) and duodenum until the tip lies 5–7 cm. beyond the duodeno-jejunal flexure. The various channels in the tube give separate access to the stomach, duodenum, and jejunum.

denum was emptied, and the entire aspirate was introduced via the appropriate lumen of the tube into the jejunum. The duodenal contents were then collected for an hour in six 10-minute samples.

In Series B and D, resting samples were collected in the same way, but the 50 ml. meal was then introduced directly into the jejunum. After the elapse of the same time interval as in Series A and C (10 minutes in all), the duodenal contents were again collected for one hour in six samples.

On all the samples, the following estimations were carried out: volume, bicarbonate concentration and total bicarbonate output per sample, enzyme concentration and total enzyme output per sample. The bicarbonate content was determined by the indirect titration technique of Lagerlof (1942), amylase by the Wohlgemuth method, trypsin by the

Lagerlof method (1942), and lipase by the technique of Cherry and Crandall. To avoid repetition, therefore, the various units referred to in the text are expressed as follows: amylase in Wohlgemuth units, trypsin in ml. N/10 alcoholic KOH, and lipase in ml. N/20 NaOH.

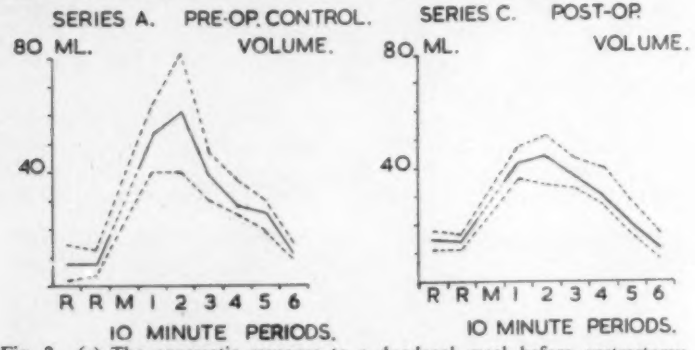

Fig. 2. (*a*) The pancreatic response to a duodenal meal before gastrectomy (Series A). (*b*) The pancreatic response to a duodenal meal after gastrectomy (Series C). Both figures show the volume of output for each 10-minute sample.
R.R. = periods for resting output.
M = period of administration of meal.

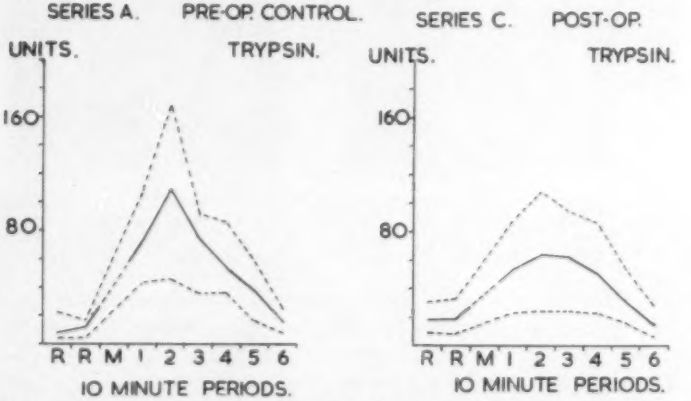

Fig. 3. (*a*) The pancreatic response to a duodenal meal before gastrectomy (Series A). (*b*) The pancreatic response to a duodenal meal after gastrectomy (Series C). Both figures show the response in total enzyme output for each 10-minute sample. The curves for trypsin are shown, but those for amylase and lipase are similar.

Results

Before proceeding to the most important feature, i.e. comparison of the various pre-operative and post-operative results, the main features of each series will be summarized.

Series A: Pre-operative pancreatic response to duodenal meal (Figs. 2(a), 3(a))

The greatest output in volume, total bicarbonate, and total enzymes occurred in the second 10-minute sample following the meal. The maximal bicarbonate concentration was seen in the third 10-minute sample, whilst the highest enzyme concentrations were recorded in the second and

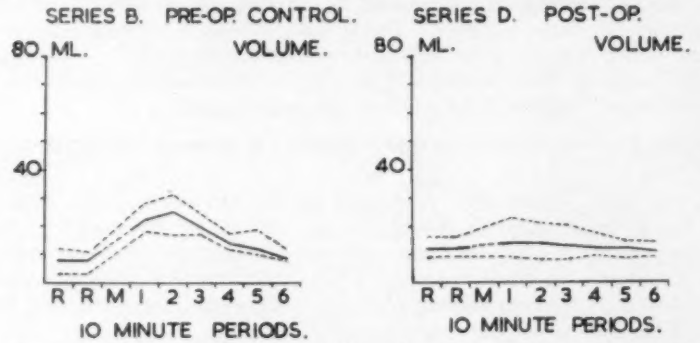

Fig. 4. (*a*) The pancreatic response to a jejunal meal before gastrectomy (Series B). (*b*) The pancreatic response to a jejunal meal after gastrectomy (Series D). Both figures show the volume of output for each 10-minute sample.

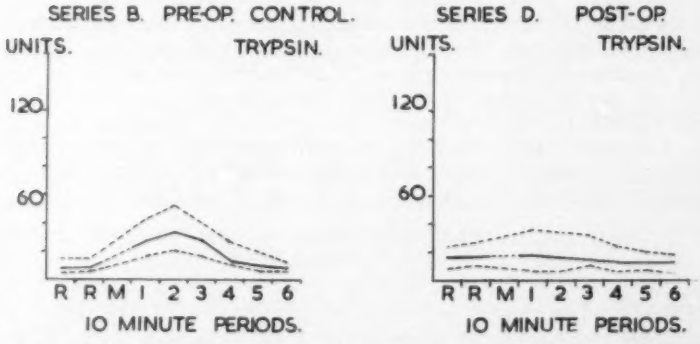

Fig. 5. (*a*) The pancreatic response to a jejunal meal before gastrectomy (Series B). (*b*) The pancreatic response to a jejunal meal after gastrectomy (Series D). Both figures show the total enzyme output (trypsin) for each 10-minute sample.

third samples. It is possible to visualize the magnitude of the pancreatic response by comparing the total output for the hour after the meal with the resting output for one hour, obtained by multiplying resting 10-minute values by six. There was a four-fold increase in volume, and a ten-fold increase in total bicarbonate output. For the enzymes, the increase was eight-fold for amylase, six-fold for trypsin, and seven-fold for lipase.

Series B: Pre-operative pancreatic response to jejunal meal (Figs. 4 (a), 5 (a))

The greatest output in volume and in total enzymes occurred most frequently in the second 10-minute period after the meal, whilst the maximum bicarbonate output was seen in the third period. As in Series A, reference to a base line, calculated from six times the resting values, showed a two-fold increase in volume and bicarbonate output, and a three-fold increase for enzyme output. The striking difference between this series and Series A is the great reduction in bicarbonate output. In general, the findings in these two series of tests are in accord with the observations of Howard (1952) in his patient with a pancreatic fistula.

Series C: Post-operative pancreatic response to duodenal meal (Figs. 2 (b), 3 (b))

The general pattern in this series showed the maximum output in volume, bicarbonate, and enzymes in the second 10-minute period. Again, by comparison with resting output, the post-operative response to a duodenal meal was as follows: There was a two-fold increase or more in volume, a five-fold increase in bicarbonate output, and a two-to-three-fold increase in enzyme output.

Series D: Post-operative pancreatic response to jejunal meal (Figs. 4 (a), 5(b))

The most obvious feature of this series was the poor response to the jejunal meal. This was shown by the flat response curves in the graphs, in the failure of the meal to increase the enzyme concentrations, and by the fact that the output of the various constituents of pancreatic secretion for the hour after the meal was similar to the resting output for one hour.

Comparison of Series A and C

This demonstrates the effect of gastric resection on the pancreatic response to food entering the duodenum, and is illustrated in Figures 2 (*a*) and (*b*), 3 (*a*) and (*b*). The differences may be summarized thus:

1. There was an increase in the resting volume of pancreatic secretion after gastrectomy. In Series A, the mean resting volume per 10 minutes was 7.85 ml. (2.4–14.2 ml.), whereas in Series C it was 14.05 ml. (10.5–18.0 ml.). This increase was seen in 45 (90 per cent.) of the patients, and in 22 (44 per cent.) the post-operative volume was greater than the maximum levels recorded in Series A.

2. The resting concentrations of bicarbonate and enzymes remained unchanged after operation. These are shown in Table I.

3. Following the meal, the alteration of the total output in volume and in the various constituents of pancreatic secretion are shown in Table II. In the post-operative series, 46 (92 per cent.) of the patients had reduced volume, and in 18 (36 per cent.) the new volume was below the minimal values in Series A.

TABLE I

MEAN RESTING CONCENTRATIONS OF CONSTITUENTS OF PANCREATIC SECRETION BEFORE AND AFTER GASTRECTOMY

	Series A	*Series C*
Bicarbonate (m/Eq./litre)	18.82	19.15
Amylase (units/ml.) ..	2,580	2,761
Trypsin (units/ml.) ..	1.2	1.28
Lipase (units/ml.) ..	114	107

TABLE II

COMPARISON OF PANCREATIC RESPONSE TO DUODENAL MEAL BEFORE AND AFTER GASTRECTOMY

(OUTPUT PER HOUR — MEAN ± S.D.)

	Pre-operative (A)	*Post-operative (C)*
Volume (ml.)	219.8 ± 15.7	183.9 ± 14.5
Bicarbonate (m.Eq.)	12.27 ± 1.47	8.20 ± 1.01
Trypsin units	364 ± 38	275 ± 61
Lipase units	38,329 ± 3,534	27,364 ± 5,778
Amylase units	1,043,950 ± 690,299	651,664 ± 231,808

STATISTICAL COMPARISON OF SERIES A AND C
(Student's t Test)

	Mean reduction	*S.D. of mean reduction*	*S.E. of mean reduction*	$t = \frac{Mean}{S.E.}$
Volume	36.07	20.4	2.89	12.48
Bicarbonate ..	4.076	1.49	0.211	19.32
Trypsin	89.30	77.0	10.9	8.19
Lipase	109.64	68.0	9.62	11.40
Amylase	392,292	293,622	41,524	9.44

($P \ll .001$).

In each case, the reduction is extremely unlikely to have happened by chance.

The bicarbonate concentrations reached post-operatively were roughly two-thirds of the pre-operative values. With reference to total bicarbonate output for one hour, all the patients showed reduced output after operation, and in 45 (90 per cent.) the post-operative level was below the lowest values in the pre-operative controls. The highest enzyme concentrations reached after operation were about half those recorded before operation. The total enzyme output for an hour was reduced following operation. In the case of amylase, 46 (92 per cent.) of the patients showed reduced output, the new level being below the pre-operative range in 20 (40 per cent.). In 45 patients (90 per cent.), the trypsin output was reduced, and in 17 (34 per cent.) this was below the minimum pre-operative value. The output of lipase was reduced in 49 (98 per cent.) of the patients, being below the pre-operative range in 22 (44 per cent.). The mean reductions were as follows:

Volume	36.07 ml.	(S.D. ± 20.4 ml.)
Bicarbonate	4.076 m.Eq.	(S.D. ± 1.49 m.Eq.)
Amylase	392,292 units	(S.D. ± 293,622 units)
Trypsin	89.30 units	(S.D. ± 77.0 units)
Lipase	109.64 units	(S.D. ± 68.0 units)

4. The bile content of the samples differed in the two groups. In the pre-operative series, the maximum bile coloration was seen in the first samples in 39 (78 per cent.) of the patients, but in Series C the bile content was greatest at the end of the hour in 36 (72 per cent.) of the patients.

Comparison of Series B and D

This comparison indicates the effect of gastric resection on the pancreatic response to food entering the jejunum directly, and is illustrated in Figures 4 (*a*) and (*b*) and 5 (*a*) and (*b*). The observed differences were as follows:

1. Again, there was an increase in the resting output in the post-operative group, i.e. a mean volume of 12.1 ml. (9–16.2 ml.) per 10 minutes in Series D compared with 7.7 ml. (2.6–12.0 ml.) in Series B. The increase was seen in 37 (74 per cent.) of the patients, and in 19 (38 per cent.) the new value was greater than the maximal pre-operative level.

2. The resting concentrations of bicarbonate and enzymes were unchanged and similar to those recorded in Table I.

TABLE III

COMPARISON OF PANCREATIC RESPONSE TO JEJUNAL MEAL BEFORE AND AFTER GASTRECTOMY

(OUTPUT PER HOUR — MEAN ± S.D.)

	Pre-operative (B)	*Post-operative (D)*
Volume (ml.)	102.4 ± 6.96	78.5 ± 10.6
Bicarbonate (m.Eq.)	2.768 ± 0.476	2.034 ± 0.401
Trypsin units	121 ± 15	89 ± 19
Lipase units	12,800 ± 1,386	8,053 ± 1,204
Amylase units	330,782 ± 72,550	187,652 ± 40,652

STATISTICAL COMPARISON OF SERIES B AND D
(Student's t Test)

	Mean reduction	*S.D. of mean reduction*	*S.E. of mean reduction*	$t = \frac{Mean}{S.E.}$
Volume	23.78	13.55	1.92	12.4
Bicarbonate ..	0.734	0.650	0.092	7.98
Trypsin	31.48	25.8	3.66	8.60
Lipase	47.46	18.5	2.61	18.18
Amylase	143,125	90,168	12,752	11.18

($P \ll .001$).
In each case, it is extremely unlikely that the reduction occurred by chance.

3. Following the meal, the total output in the two series is given in Table III. With reference to the volume for one hour, 48 (96 per cent.) of the patients showed a reduction in Series D, and in 38 (78 per cent.) the post-operative volume was less than the minimum observed in the pre-operative series. The bicarbonate and enzyme concentrations recorded in the post-operative series showed minimal variation following the meal. The total bicarbonate output for one hour was reduced in 46 (92 per cent.) of the patients after operation, being below the lowest values in Series B in 24 (48 per cent.). The total amylase was decreased in 48 (96 per cent.) after operation, and was below the range observed in Series B in 41 (82 per

cent.) of the patients. A reduced output of trypsin was seen in 45 (90 per cent.) of the patients post-operatively, and in 39 (78 per cent.) the value was below the pre-operative range. The lipase output was found to be reduced in all of the patients post-operatively, 48 (96 per cent.) having an output below the pre-operative level. The mean reduction of each component was as follows:

Volume	23.78 ml.	(S.D. $\pm$ 13.55 ml.)
Bicarbonate	0.734 m.Eq.	(S.D. $\pm$ 0.65 m.Eq.)
Amylase	143,125 units	(S.D. $\pm$ 90,168 units)
Trypsin	31.48 units	(S.D. $\pm$ 25.8 units)
Lipase	47.46 units	(S.D. $\pm$ 18.5 units).

4. The maximum bile coloration was again observed in the early samples in Series B, but later samples in Series D.

Statistical analysis

Since the same patients were subjected to tests in each series, it is permissible to apply statistical criteria to the mean reductions already given. " Students t test " was used, and the differences noted between Series A and C, and between Series B and D, were significant ($P. \ll 0.001$).

Conclusions

It is evident that one effect of gastrectomy on pancreatic function is to increase the resting rate of secretion. This may account for " le secretion de compensation " observed by Fried and Stein (1923). A second effect of the operation is a delay in the appearance of bile in the duodenal contents following meals. This observation is in agreement with the findings of Roux *et al.* (1950) and Lundh (1958).

With reference to the response to food entering the duodenum after operation, i.e. as in the Billroth I patient, the pancreatic output in one hour following the meal is approximately two-thirds or three-quarters of the pre-operative output. Not only is the volume reduced, but the highest concentrations of bicarbonate and enzymes reached are less than those occurring normally.

When the duodenum is by-passed and food enters the jejunum directly, the pancreatic response is modified by gastrectomy in a different manner. In this case, the pancreas continues to secrete at its new resting rate. By inference, this must resemble the pattern of response to be expected after Polya operations.

The main problem concerns a possible explanation of these findings. According to the present concept of the control of pancreatic secretion, there is an unimportant psychic phase, no gastric phase, an all-important intestinal phase involving the secretin-pancreozymin combination, and an uncertain degree of control by the vagus. It is unlikely that altered hormonal release is responsible for the changes seen post-operatively,

since the same meal was given under the same conditions before and after operation. A possible clue to the explanation was afforded when a few patients, who had vagotomy alone, were investigated by intubation tests similar to those described. The results are shown in Figure 6 (*a*) and (*b*), which illustrate the pancreatic response to a duodenal meal and a jejunal meal. The similarity of the responses to those recorded in Series C and D suggests that vagal section, coincident with gastrectomy, may contribute to the modification of the pancreatic response occurring after gastrectomy.

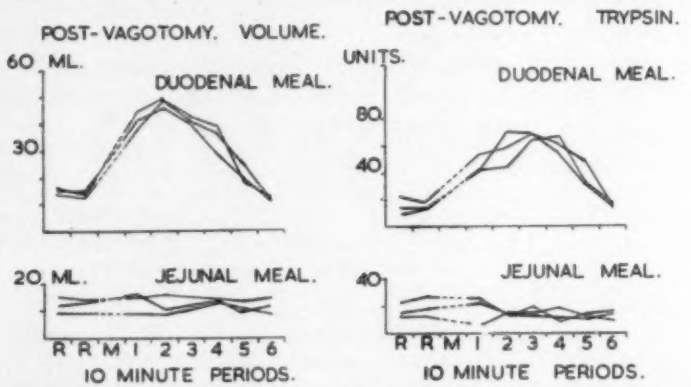

Fig. 6. (*a*) Pancreatic response (volume) after vagotomy. The upper curves show the response following a duodenal meal; the lower curves show the response following a jejunal meal. (*b*) Pancreatic response (total trypsin output per sample) after vagotomy. The upper curves show the response following a duodenal meal; the lower curves show the response following a jejunal meal.

It is very difficult indeed to be precise about the vagus. Vagotomy may affect the pancreas in several ways. In the first place, there may be section of the nerve supply to this organ. Secondly, the motility, secretion, and perhaps release of hormones from the duodenum and jejunum may be altered by denervation. Finally, afferent pathways may be divided, and the pancreas may be deprived of the effects of reflexes (Harper, 1959). Nevertheless, comparison of the pre-operative control responses, as shown in Series A and B, with the post-vagotomy curves does indicate that vagal integrity may confer on the pancreas the versatile response recorded when food enters the duodenum normally. Further, an intact vagus seems to be necessary to potentiate weaker stimuli arising in the jejunum when food is introduced directly. In passing, it may be stated that these observations favour the practice of vagotomy combined with pyloroplasty rather than with gastro-enterostomy in the treatment of duodenal ulcer. On the other hand, they may indicate a physiological background for the work of Burge (1960) in his endeavour to preserve the pancreatic nerve supply from the vagus.

It must be stressed that there are several other factors which may be important after gastrectomy. The normal stomach discharges its contents into the duodenum in small amounts, and this almost certainly results in a sustained output from the pancreas, which continues until the stomach is empty. Following gastrectomy, rapid emptying of the gastric remnant may lead to a pancreatic output of short duration. In addition, the proximal intestine empties very rapidly after gastrectomy (Bruusgaard, 1946; Lundh, 1958), and this factor may certainly reduce hormonal release. The duodenum following a Polya operation is constantly bathed in alkaline fluid. This may depress pancreatic secretion. Finally, since some of the post-cibal syndromes occurring after operation are mediated by the sympathetic nervous system, pancreatic secretion may be reduced further if the reflex arcs involve the pancreas. All of these factors, however, would accentuate the altered pancreatic secretion observed in the intubation experiments.

The evidence shows that considerable modification of the pancreatic response to food follows gastrectomy. It now remains to correlate this with observations on post-gastrectomy steatorrhoea.

PART II

THE PATTERN OF STEATORRHOEA FOLLOWING GASTRECTOMY

Whilst the previous investigations were in progress, a study was made of the pattern of steatorrhoea following various types of gastric operation, the aim being to provide information which might assist in the evaluation of the intubation tests. Routine faecal fat analyses were done over a period of seven years, and these results form the basis of this part of the lecture. A review of the complicated problem of fat absorption and steatorrhoea in general is beyond the scope of this paper. It will be sufficient to indicate that the basis of our understanding in this matter is the " Partition Hypothesis of Fat Absorption " (Frazer, 1958).

A review of the literature on post-gastrectomy steatorrhoea

There is general agreement that steatorrhoea is common after subtotal gastrectomy. From the literature, it has been estimated to occur in about 60 per cent. of patients (Butler *et al.*, 1954). Usually the steatorrhoea is not associated with symptoms, but occasionally it may contribute to a fully developed mal-absorption syndrome with creatorrhoea, hypoproteinaemia, avitaminosis, and anaemia (Seip, 1950; McPhee, 1953; Frankel and Moore, 1953; Naish and Capper, 1953; Bruce, 1955). The incidence of this severe state is less than 1 per cent., as seven cases have been seen in a personal review of approximately 800 Polya gastrectomy patients during the past 12 years. All the affected patients had antecolic anastomoses, and the earliest presentation was five years after operation. The majority developed the syndrome between seven and eleven years afterwards, and this delayed appearance is an important feature of the condition.

A great deal of work has been done to demonstrate the frequency and severity of steatorrhoea after various types of gastric operation. In animals, the main contributions have been by Welbourn *et al.* (1953), Jarvid (1955), and Everson (1955), whilst in man, Wollaeger (1946, 1950), Wallensten and Gothman (1953), Everson (1954), and Robins (1957) have made valuable reports. From these studies, several facts have emerged, and these may be summarized as follows:—

(*a*) Steatorrhoea seldom occurs after gastro-enterostomy.
(*b*) It seldom follows vagotomy alone.
(*c*) It is rare after the Billroth I operation.
(*d*) It is common after the Polya operation.
(*e*) It is the rule after total gastrectomy.
(*f*) The addition of vagotomy to gastrectomy increases fat loss in faeces.

The general impression given by analysis of faeces is that fat absorption is disturbed more frequently and to a greater extent than protein absorption. The intubation studies of Lundh (1958), however, have shown that the absorption defect following gastrectomy is greater for protein than for fat.

The present study of post-gastrectomy steatorrhoea

Since 1953, a simplified technique for the identification of steatorrhoea has been used in Frenchay Hospital (Woodman and Yeoman, 1955). Faecal fat analyses were carried out on patients taking an ordinary hospital diet, which contained approximately 70 G. of fat daily. The 24-hour output of faeces from each patient was collected in a container, which was sealed, labelled, and dispatched to the laboratory. The procedure was repeated over three successive periods of 24 hours. The individual specimens were homogenized according to the method of Anderson *et al.* (1952), and the fat content was estimated by the technique of Van de Kamer *et al.* (1949). For each patient, the faecal fat content was expressed as grammes of fatty acid per sample, either as a mean 24-hour value or as a total three-day excretion.

Recently, it has been suggested that the original fat balance techniques, valuable though they were, gave a false idea of accuracy. Monasterio *et al.* (1953), Cooke (1956; 1958), and Frazer (1955; 1958) have indicated that a simple record of faecal fat, usually over a period of three days, expressed as grammes of fatty acid per day, is sufficient.

In normal control patients, the findings with the method used in this study were as follows:—

(i) Mean daily fat excretion: 3.91 $\pm$ 2.45 G. fatty acid.
(ii) Mean three-day fat excretion: 11.72 $\pm$ 3.17 G. fatty acid.

According to these analyses, the upper limit of normal for three days is 18.06 G., which is similar to that suggested by Cooke (1956; 1958), i.e. an excess of 18 G. per three days (6 G. daily) is indicative of steatorrhoea. In the present series, therefore, patients were grouped in the simplest possible manner—those with a normal three-day fat excretion of 18 G. or less, and those with steatorrhoea having more than 18 G. per three-day period.

The incidence of steatorrhoea was studied after several types of gastrectomy, the number of patients in each group being as follows:—

(*a*) Billroth I Gastrectomy 86
(*b*) Ante-colic Polya Gastrectomy (Balfour) .. 127
(*c*) Retro-colic Polya Gastrectomy 81

In addition, some patients who had conversion operations of one type of gastrectomy to another were investigated in the same way.

TABLE IV

INCIDENCE OF STEATORRHOEA AFTER GASTRIC OPERATIONS

		Number with Steatorrhoea	
		3 months	*3 years*
Operation	*Number*	*Post-operative*	*Post-operative*
Billroth I	86	1 (1%+)	7 (8.1%)
Ante-colic polya	127	77 (61%)	93 (73%)
Retro-colic polya	81	16 (20%)	27 (33%)

As a general rule, the fat analyses were carried out on two separate occasions. The first was done two or three months after operation, when the patient was on a near-normal meal frequency and ready to return to his or her normal occupation. The second analysis was carried out approximately three years after operation. This was done to see if there was any change in the original incidence of steatorrhoea.

Results

The incidence of steatorrhoea following the various types of gastrectomy is shown in Table IV. Figures 7, 8 and 9 show the distribution of the results in the three main groups of patients, i.e. with Billroth I, Ante-colic Polya, and Retro-colic Polya operations respectively. It will be seen that steatorrhoea is rare following the Billroth I operation, but common after Polya operations, especially in patients with long afferent loops. The most interesting feature, however, is the increased incidence of steatorrhoea with the passage of time. This increase is of the same order in all groups, and is significant ($P < .05$).

The abolition of steatorrhoea by the conversion of a Polya anastomosis to a Billroth I type is well established, and is illustrated in Figure 10. Perhaps a more interesting type of conversion, however, is the change from a long ante-colic Polya anastomosis to one with a short retro-colic loop. During recent years, a few patients have been referred with recurrent ulceration, either anastomotic (jejunal) ulcers or gastric ulcers

in the stomach remnant. The previous operation was a Balfour gastrectomy in each case. Secondary gastrectomy was indicated for those with new gastric ulcers, but vagotomy could have been done for those with jejunal ulcers. In view of the adverse effects of adding vagotomy to

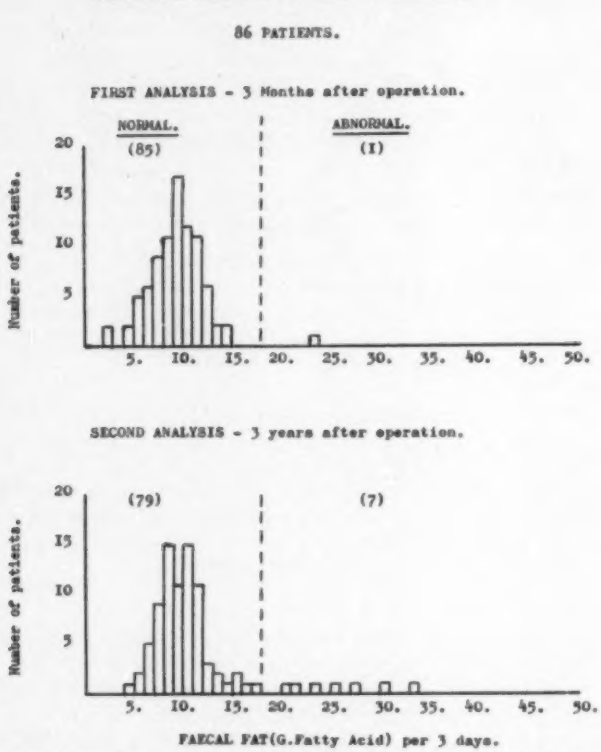

Fig. 7. The distribution of normal and abnormal faecal fat values in patients following the Billroth I operation.

gastrectomy, with increased weight loss and steatorrhoea, an alternative procedure was carried out based on the following principles:

(1) The amount of stomach resected should be adequate.

(2) A piece of jejunum, as high as possible, should be used for the anastomosis because of its increased resistance to ulceration.

(3) The afferent loop should be as short as possible, so that the contents retain their buffering capacity (Cross, 1952).

The operation consequently consisted of a secondary gastrectomy, but the new anastomosis was made as close as possible to the duodeno-jejunal flexure, in a manner closely resembling the operation described by Hermon Taylor (1959a). The effect of such a conversion in 11 patients is shown in Figure 11.

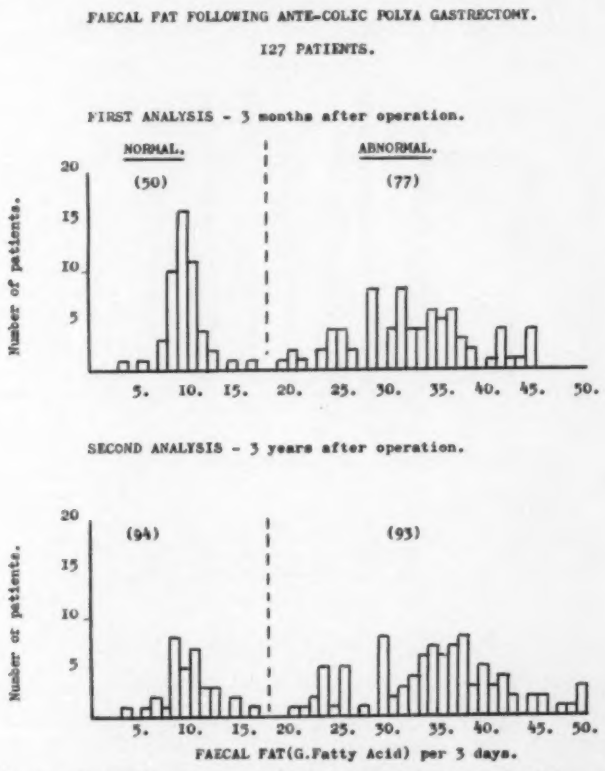

Fig. 8. The distribution of normal and abnormal faecal fat values in patients following Polya operations with long afferent loops.

These results confirm much that has been observed already—the more frequent occurrence of steatorrhoea following the Polya operation than the Billroth I procedure. In addition, there is support for the contention of Stammers (1955) that steatorrhoea is more likely to occur in patients with long ante-colic loops compared with those with short retro-colic loops. This is illustrated, not only by the Figures 8 and 9, and Table IV, but also by the beneficial effect of shortening the afferent loop in the con-

version operations. Hermon Taylor (1959b) believes that steatorrhoea does not occur following his " no loop " operations, and O'Connell of Dublin (1955) has reported a similar finding in his patients with a Roux-en-Y anastomosis. It seems certain, therefore, that the presence of the afferent loop and its length are factors of importance in the causation of

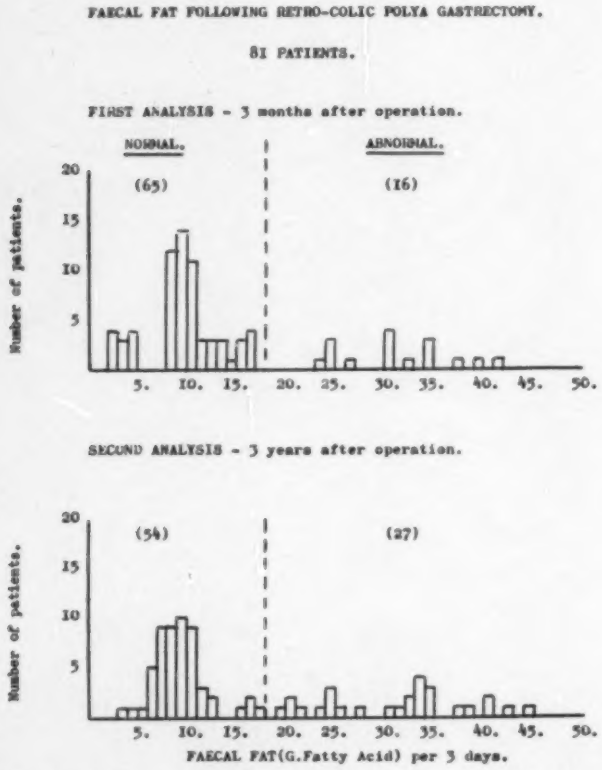

Fig. 9. The distribution of normal and abnormal faecal fat values in patients following Polya operations with short retro-colic afferent loops.

post-gastrectomy steatorrhoea. On the other hand, the increased incidence of steatorrhoea with the passage of time indicates the presence of other factors, because the increased incidence was observed in patients without afferent loops, i.e. those with Billroth I operations. It must be pointed out that this observation differs from that of Welbourn *et al.* (1953) in dogs and that of Polak and Pontes (1956) in man.

The enzyme concentration of afferent loop contents

On the basis of the concept that enzyme estimation in intestinal contents is the only valid method of determining whether or not a deficiency of pancreatic secretion is responsible for an abnormality in the faeces, further enzyme studies were done in patients following a Polya gastrectomy. In cases of known pancreatic defect, variations in enzyme output are so great that actual absence of enzymes is the only finding of value (Dorn-

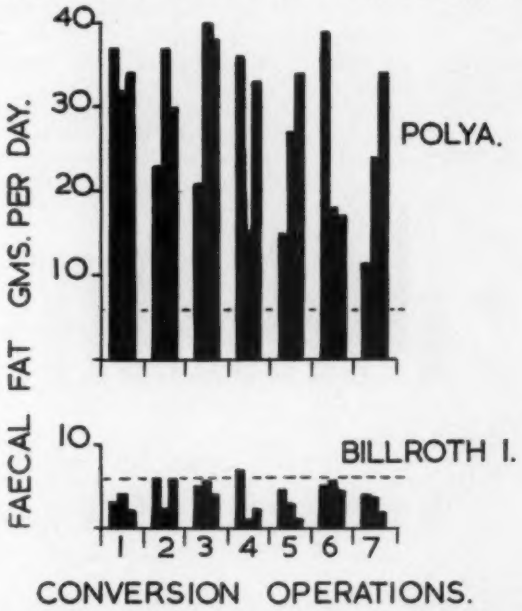

Fig. 10. The effect of conversion of a Polya anastomosis to Billroth I, showing the change in the faecal fat values.

berger, *et al.* 1948; Dreiling, 1953). An attempt was made, therefore, to determine the presence or absence of enzymes in afferent loop contents as they passed into the main intestinal pathway.

It is generally recognized that the afferent loop empties irregularly, the evidence being both clinical and radiological. Consequently, it was decided that single estimations of enzymes would not give a true picture, and samples were collected from each patient on three different occasions.

Investigations were carried out on the ante-colic and retro-colic groups of Polya patients. In the first group, 30 with steatorrhoea and 30 controls with normal faecal fat values were studied, affording 90 estimations of

each enzyme in the test patients and in the controls. There were no criteria of selection. The 16 patients with steatorrhoea in the retro-colic group were also studied, together with 16 control patients. In this group there were, therefore, 48 estimations of each enzyme in the test and control patients.

A Levine's tube was passed through the nose in each patient into the gastric remnant, and then positioned radiologically so that the tip lay in the efferent loop just beyond the stoma. The patients were encouraged to take their meals during the day, and three samples of afferent loop contents were collected after the meals. One sample was collected after each of three meals in every patient.

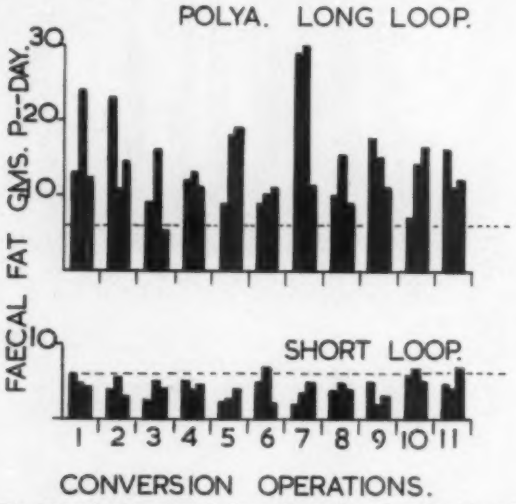

Fig. 11. The effect of conversion of a long afferent loop to a short loop in patients with Polya operations, showing the change in faecal fat values.

The results are depicted in Table V. Throughout, amylase was present in excess of 1,000 Wohlgemuth units per ml. In patients with ante-colic anastomoses, both trypsin and lipase were found to be absent more frequently in those with steatorrhoea compared with the controls. In patients with retro-colic anastomoses, trypsin was present in all the estimations, but lipase was absent more frequently in the steatorrhoea group compared with the control patients. Statistically, these observed differences are significant.

Following intubation studies on patients who had had a total gastrectomy, Brain and Stammers (1951) stated that enzymes were present, but they gave no further details. My own results are in agreement with the

findings of Kiekens and Lundh (1957) and Lundh (1958), who observed reduced concentration of enzymes and also absence of trypsin occasionally. These authors estimated trypsin concentration only.

The simplest explanation of the findings, and probably the correct one, is that the differences are due to the relative instability of the various enzymes. Lipase is known to be the most unstable and most readily inactivated, especially in the presence of trypsin. Trypsin itself is also unstable, whilst amylase is by far the most stable. The longer the enzymes stay in the afferent loop, the greater is the risk of lipase becoming inactivated—and possibly trypsin also. It is reasonable to suspect that this risk is increased in patients with long ante-colic afferent loops compared with those with short retro-colic loops. It is possible that vagotomy makes a contribution by increasing afferent loop stasis and delaying effective emptying of the afferent loop. The advent of infection, too, may produce inactivation of the enzymes during stasis.

TABLE V

FREQUENCY OF ABSENCE OF ENZYMES IN AFFERENT LOOP CONTENTS

Ante-colic Polya patients	*Controls* (30)	*Steatorrhoea Group* (30)
Lipase (90 tests)	7 (7.7%)	33 (36.6%)
Trypsin (90 tests)	3 (3.3%)	16 (17.7%)
Amylase (90 tests)	0	0

Statistical analysis: (x^2). For lipase $P \ll .001$
(x^2). For trypsin $P < .005$

Retro-colic Polya patients	*Controls* (16)	*Steatorrhoea Group* (16)
Lipase (48 tests)	0	14 (29.2%)
Trypsin (48 tests)	0	0
Amylase (48 tests)	0	0

Statistical analysis: (x^2). For lipase $P < .001$

It is now possible to describe an over-all picture of the pattern of steatorrhoea following gastrectomy as a result of all the findings reported.

Initially, steatorrhoea is rare following the Billroth I operation, occurring in just more than 1 per cent. of patients. It is common following the Polya gastrectomy, but occurs more frequently in patients with long ante-colic anastomoses (61 per cent.) than in those with short retrocolic anastomoses (20 per cent.). Following any of these operations, there may be an increased incidence of steatorrhoea with the passage of time, approximately a further 10 per cent. of patients developing steatorrhoea. In patients with Polya anastomoses, procedures which abolish the afferent loop, shorten it, or improve its drainage, have a beneficial effect in that they reduce the severity of the steatorrhoea.

There is evidence that inactivation of some of the pancreatic enzymes occurs in the afferent loop in patients following Polya gastrectomy. This

inactivation involves lipase especially, and is seen more frequently in patients with steatorrhoea than in those with normal fat excretion. In addition, the enzyme inactivation occurs more often in patients with long afferent loops compared with those with short loops, and this is associated with a difference in incidence of steatorrhoea.

DISCUSSION

Perhaps the most satisfactory basis for discussion of the findings is that provided by the existing concepts of the causation of post-gastrectomy steatorrhoea. Several reasonable hypotheses have been suggested, and, although each represents a particular facet of the problem, one cannot exclude either the summation of several factors in any one patient or different causes operating in different patients. The various concepts may be summarized as follows:

(*a*) *Loss of reservoir function of the stomach* (Warren, 1954; Avery Jones, 1959). This is certainly a real factor, because the absence of a gastric reservoir permits large particles of food to enter the intestine, the particles being too large for easy breakdown by enzymes. It may be contended that the reservoir function of the stomach is more important for fat than for other food substances. The best support for this particular hypothesis is afforded by the improvement in nutrition when small meals are given frequently. This obviously simulates the normal state of affairs in which small amounts of food enter the intestine at intervals. The benefit of this fractionation of meals has been demonstrated in man and animals (Brain and Stammers, 1951; Warren, 1954; McCorkle and Harper, 1954; Emery, 1935; Lepore, 1956).

(*b*) *Poor mixing of food, bile and enzymes.* Much support for this belief can be found in the literature (Warren, 1954; MacLean *et al.*, 1954; Kelly *et al.*, 1954; Wells, 1955; Polak, 1956; Kiekens and Lundh, 1957; Lundh, 1958). Brain and Stammers (1951) suggested the phrase " pancreatico-cibal asynchrony " to signify that the necessary hormonal and nervous stimuli reached the pancreas too late after the meal had entered the intestine. To my mind, Lundh (1958) demonstrated the truth of this concept quite conclusively by his intubation studies. A large part of the meal passed on through the intestine without mixing with pancreatic enzymes or bile. On the other hand, the experiments of Welbourn (1954) indicated that failure of mixing of food and enzymes was not the complete answer. He showed that there was little difference in fat loss following oesophageo-duodenostomy and oesophageo-jejunostomy. At this juncture, one may recall the work of Hertel (1929–30), who showed that, although chyme and bile were not mixed in the proximal intestine following gastrectomy in dogs, the state of digestion in the terminal ileum was similar to that seen in animals with an intact stomach, indicating adequate compensation by the intestine. Commenting on these observa-

tions, Lundh (1958) considered that bacterial activity was responsible for the final state of digestion rather than pancreatic enzymes, as these were progressively inactivated as they passed along the intestine.

(*c*) *Pancreatic deficiency.* Gavrilla (1929) and Dreiling (1957) have expressed the view that pancreatic insufficiency is responsible for steatorrhoea in the present context. Although the work of Shingleton *et al.* (1957) and Ruffin *et al.* (1958), using radio-active labelled fat techniques, has been interpreted in support of poor mixing of pancreatic enzymes, an equally reasonable view would be that it indicated the presence of a pancreatic defect. Kiekens and Lundh (1957) and Lundh (1958) have shown that there is reduced enzyme concentration, and even occasional absence of enzymes, following gastrectomy. Shingleton *et al.* (1957) claimed that the administration of pancreatic extract and bile corrected the steatorrhoea following gastrectomy in man, but Johnston and Welbourn (1958) were unable to confirm this in dogs. In general, corrective treatment planned to remedy deficiencies, e.g. pancreatic extracts, bile, emulsifying agents, has yielded disappointing results (Warren, 1954; Welbourn *et al.* 1953; Ward-McQuaid, 1949; Ellison, 1955). This is in marked contradistinction to the benefit given by pancreatic extracts in patients with known pancreatic defects, e.g. following pancreatectomy.

(*d*) *Rapid transit through the intestine.* Very rapid transit of food through the intestine has been incriminated by some authors, but it is difficult to evaluate its importance. Indeed, recent studies by Cummins and Almy (1953) have indicated that increased intestinal motility is associated with increased absorption. Unfortunately these experiments were done with only glucose and methionine. Wells and Welbourn (1951) considered that the speedy entrance of food into the intestine increased peristaltic activity, and Ferris *et al.* (1943) showed that increased transit through the intestine occurred after gastrectomy. Some of the phenomena of the "dumping syndrome" are believed to be due to increased intestinal motility (Jordan *et al.*, 1957), and Wollaeger (1950) has shown that patients with this syndrome lose more fat in the stools than asymptomatic controls. Further, the use of atropine (Wollaeger, 1950) and hexamethonium bromide (Welbourn and Glazebrook, 1952) to reduce the speed of transit of food through the bowel resulted in a reduction in the degree of steatorrhoea. On the other hand, Freeman *et al.* (1943) in monkeys and Bruusgaard (1946) in man have shown that rapid movement occurred in the proximal intestine after gastrectomy, but that there was compensatory slowing in the distal intestine.

(*e*) *Blind loop syndrome.* The fully developed malabsorption syndrome occasionally following gastrectomy is very similar to that seen after intestinal surgery with the formation of a blind loop. On this basis, Naish and Capper (1953) and Butler *et al.* (1954) suggested that the "cul-

de-sac " of the afferent loop might contribute to the causation of steatorrhoea. Witts (1955) indicated that high intestinal loops may be associated with steatorrhoea. Abolition of the afferent loop by conversion of the Polya anastomosis to one of the Billroth I type corrects the steatorrhoea (Butler *et al.*, 1954; Bruce, 1955). Card (1959), however, did not consider that the contents of the loop were truly stagnant, the loop being washed through by pancreatic secretion and bile. Nevertheless, there is little doubt that the malabsorption state in the patients described by Capper and Naish was a " blind loop syndrome ".

(*f*) *Latent defects.* This concept of post-gastrectomy steatorrhoea raises the most interesting possibilities. One must not overlook the fact that gastrectomy, with the resultant increased load on the intestine, may bring into relief some other latent defect. This may be a mild pancreatic deficiency (Marks and Tompsett, 1958; Bruce, 1959) or an intestinal defect like ideopathic steatorrhoea (Forshaw, 1958; Shiner, 1959; Pauley, 1959). This possibility of gluten-induced enteropathy may be very important. In this condition, the causative agent is dietary wheat. Acid hydrolysis and de-amination remove the deleterious effects of the compound, but these effects may persist after peptic and tryptic digestion. Therefore, following gastric resection and loss of acid, the intestine may be exposed to the effects of gluten.

The evidence in favour of an intestinal absorption defect is not yet fully convincing. Benson *et al.* (1957) believed that the results of the D-Xylose absorption test indicated defective absorption after gastrectomy, and Shingleton *et al.* (1957) and Ruffin *et al.* (1958) demonstrated poor absorption of fatty acids in some of their patients. On the other hand, the folic acid excretion test gives normal results in patients following gastrectomy (Cox *et al.*, 1958). Jejunal biopsy, too, has not afforded much assistance. Shiner (1958, 1959) and Lees and Grandjean (1958) have reported normality of jejunal mucosa after gastrectomy. Baird and Dodge (1957) found evidence of superficial inflammation in specimens of jejunal mucosa in two of five patients with post-gastrectomy steatorrhoea, and concluded that the jejunal changes were not important. Pauley (1957, 1959) maintained that the jejunal change may be patchy, and that biopsy results must be interpreted with caution.

(*g*) *Alteration of intestinal flora.* Under normal conditions, organisms cannot be found in the small intestine (Girdwood, 1959). Following gastrectomy, organisms ascend into the small intestine (Wells and Welbourn, 1951; Heller, 1956). It must be stressed, however, that this increased bacterial activity in the small intestine may be largely dependent on a defect of absorption. If small intestinal absorption is normal, practically no dietary assimilable material passes into the large intestine, and bacterial growth in the colon is consequently restricted by this adverse

nutritional condition (Frazer, 1955). It appears, therefore, that some defect in absorption precedes the alteration of intestinal flora, but, once this change has occurred, further absorption defects and stool changes may be produced.

With reference to my own results, it will be recalled that the pancreatic response to food entering the duodenum after gastrectomy was considerable, although reduced compared with pre-operative standards. This output, which would be expected following a Billroth I gastrectomy, is almost certainly adequate for normal digestion. This is demonstrated by the fact that only one patient in the series of 86 had steatorrhoea immediately following operation. All the patients who developed steatorrhoea later had a good pancreatic response to food, and the occurrence of the steatorrhoea cannot be explained on the grounds of pancreatic defect. It is submitted that these patients may be included amongst those in whom operation brings to light a latent defect. The incidence of the delayed steatorrhoea, seven of the 86 patients, closely resembles the incidence of jejunal abnormality reported by Pauley (1957) in his gastrectomy series (five in 61). The other possibility, of course, is that the late cases may be due to a gradual change in the bacterial content of the intestine.

The pancreatic response to food entering the jejunum following gastrectomy, i.e. the response to be expected in patients with a Polya gastrectomy, is characteristically flat. It cannot be stated with certainty that this response is adequate for normal digestion and absorption. My experience of patients with chronic pancreatitis, although very limited, leads me to believe that if a similar output was recovered from a patient with chronic pancreatic disease, steatorrhoca would not be present. It is arguable, therefore, that the pancreatic output following a Polya operation is adequate but probably borderline. The real problem after this operation is one of access—the enzymes are retained in the afferent loop and, as Lundh has shown, never reach a large part of any meal. Further, the investigations have shown that inactivation of lipase may occur frequently, and inactivation of trypsin occasionally. The frequency or degree of inactivation is related to the length of the afferent loop. Presumably such a defect affecting lipase in particular would cause a reduction in the absorption of particulate fat, and explain the results reported by Shingleton and Ruffin using isotopic triolein.

The increased incidence of steatorrhoea with the passage of time was also apparent in Polya patients. It is interesting to observe that the increase is of the same order. Once again a latent defect in the gut may be responsible, or a blind loop syndrome may develop slowly.

It is possible, however, that the problem of bacterial activity assumes greater importance in this group. The presence of a gross defect of

absorption at the outset must lead to favourable conditions for increased growth of organisms. This, in turn, may produce further upset of absorption and abnormality of the faeces. The advent of infection into the afferent loop would augment the inactivation of enzymes. Indeed, the use of antibiotics, and of chlortetracycline in particular, reduces the steatorrhoea in patients with severe post-gastrectomy malabsorption.

The flat response reported in Polya patients has a practical significance. Since the pancreas cannot respond to food by increased output, then the meals should be reduced in amount and given frequently. This would enable the pancreatic secretion to deal more adequately with the meals. In addition, it is essential that the afferent loop should be made as short as possible.

There is one more point worthy of mention, and possibly needing further study. It is believed that bile salts are absorbed least in the duodenum and maximally in the ileum (Everett, 1948). According to Borgstrom *et al.* (1957), the available pool of bile salts is circulated twice during digestion. Polak (1956) observed that fat absorption after gastrectomy could be improved by the administration of bile. It may be that bile salts, held in the afferent loop and not in use, are absorbed. When the afferent loop empties, a suitable milieu with a bile salt concentration of 1–3 mgms. per ml. may not be produced for digestion.

Conclusion and summary

It is evident that there is no question of pancreatic deficiency following the Billroth I operation. Steatorrhoea is not a feature of the immediate post-operative period, but develops after an interval. It is reasonable to suspect, therefore, that the steatorrhoea is attributable to either a pre-existing latent intestinal defect, which is brought to light by the operation, or alternatively is related to a change in the intestinal flora following the operation.

In contrast, steatorrhoea is seen immediately following the Polya operation. There is evidence of a gross reduction in pancreatic output and of inactivation of enzymes in the afferent loop. It is not possible to attribute the steatorrhoea to one factor. In addition to the loss of the reservoir function of the stomach, the problem seems to be one of accessibility. The pancreatic secretion, reduced as it is, is retained for varying periods in the afferent loop and cannot mix adequately with food. The inactivation of lipase aggravates the situation further. With the passage of time, latent intestinal defects may become apparent, but the increased bacterial activity in the intestine may assume a very important role in the production of steatorrhoea and more severe states of malabsorption.

ACKNOWLEDGMENTS

I would like to record my especial gratitude to the late Dr. Dorothy Woodman, formerly Director of the Laboratories at Frenchay Hospital, to her successor, Dr. R. D. Eastham, and to Mr. W. B. Yeoman, the Bio-

chemist at the Hospital. Every possible laboratory facility was placed at my disposal, and without this co-operation the entire work would not have been possible.

In addition, all my colleagues gave invaluable help and encouragement throughout the whole period, and to these I tender my sincere thanks:

(1) The members of the Radiological Department at Frenchay Hospital.

(2) The Ward Sisters and Nurses, without whose aid we could achieve very little.

(3) Miss E. H. L. Duncan, M.A., B.Sc., for invaluable help with the statistical analyses.

(4) Miss G. Allen for secretarial assistance.

Finally, I would like to express a word of praise and thanks to all those patients who have helped me by their unfailing co-operation at all times.

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A VISIT TO KHARTOUM

A résumé of the Report
by
Professor F. A. R. Stammers, C.B.E., T.D., Ch.M., F.R.C.S.
to
The Committee of Management of the Examining Board in England
19th June 1961

AT THE REQUEST of the Committee of Management of the Examining Board in England of the Royal College of Physicians of London and the Royal College of Surgeons of England, and on the invitation of the University of Khartoum, supported by the Ministry of Health of the Republic of the Sudan, I acted as Visitor to the Faculty of Medicine and attended the pre-clinical and clinical examinations, including the Finals, for the M.B., B.S. (Khartoum).

The general pattern of the programme arranged for the Visitor was, as in previous years, that during the first few days he meets the leaders and heads of departments of the University and the Ministry of Health, the Medical Director and Staffs of the civil hospitals, and the Director and members of the Stack Laboratory. These conversations helped to paint a picture of the background against which the health of the people was cared for, and revealed the great upsurge of enthusiasm and energy with which the leaders were trying to build up better services and opportunities for the people. After this he visits various parts of the country, in my case the Gezira and Equatoria, in order that he may see for himself the conditions under which medical work has to be carried out in the Sudan. Finally, he attends the examinations, once again mixing with the members of the different Departments of the Medical School and Hospital, meeting the External Examiners and, especially, observing the general performance of the students. I would like particularly to thank Professor H. Butler, Dean of the Faculty of Medicine and Professor of Anatomy, who, together with members of the Ministry of Health, organized the whole tour and made it possible for me, within a few weeks, to gain such a comprehensive view of this vast country with a population of 11,500,000 people, and to get to know so many of the men who are responsible for the medical services.

Travelling the country was most instructive; indeed, in spite of the detailed descriptions given to me during the first few days, it is really impossible to imagine the real environmental circumstances until one has visited different parts of the country. Having spent two years of my War service in another part of tropical Africa I was partly prepared for the profound influence that climate, widespread tropical diseases, malnutrition, poor communications and illiteracy have on the organization of medical services; and when are added the primitive state of some of the tribes in the south, the nomadic habits of some of the population elsewhere

and the steady stream of pilgrims from other African States crossing the western boundaries of the Sudan on their slow journey to Mecca, sometimes bringing active disease with them, one realizes that these factors dominate the situation. At any time, and of a sudden, epidemics of killing disease such as yellow fever, sleeping sickness or cerebro-spinal meningitis, will strike wide areas. Malaria is widespread in the south and bilharzia and madura in the north, whilst tuberculosis of the florid kind affecting several systems in the same patient at the same time is common everywhere; in smaller numbers, so too is leprosy. Yet there are only 250 doctors, and since a large proportion of these are in the Three Towns, this means about 1 to 70,000 or 80,000 people. Under such circumstances, the first and most effective line of defence against these devastating diseases is prevention and this lies in hygiene and public health measures; indeed, at this stage of the country's development it is true to say that more lives can be saved by preventive measures than by the most advanced medicine and surgery, and that only as more doctors become available can the victims receive full treatment. In addition, of course, there are plenty of conditions besides tropical ones requiring the services of fully trained doctors. The organisation of the medical services was described in detail and with great accuracy by the Visitor of last year. He made special reference to the medical assistants, giving them high praise, and the present Visitor was equally impressed. They are recruited from male nursing orderlies, and selected for their knowledge, intelligence and integrity, and then given more advanced training for a further two years. They are completely devoted to their work, and it is interesting to see how greatly the P.M.O.Hs. (Provincial Medical Officers of Health) and Assistant P.M.O.Hs. depend on their services. Apart from Public Health the shortage of specialists is even more acute, and although the authorities are willing to transport patients requiring major surgery to Khartoum by air, immediate skilled treatment is just not available for many of the emergencies, including fractures. Even at Juba, with its Hospital of over 400 beds, there has not been a surgical specialist for several years, and the present gynaecologist is the first for six years. It should be added that transportation by ambulance or car over desert tracks, the surface of which becomes corrugated so that the vehicle shakes and rattles as it goes along is, for an acutely ill patient, a traumatizing experience.

KHARTOUM

Khartoum consists, as the official guide book puts it, of three bridge-linked towns—Khartoum, Khartoum North and Omdurman. Omdurman is, in fact, the largest town in the country, and consists almost entirely of native houses—though some handsome official buildings have recently been added—and has the largest native market in the Sudan. Khartoum, on the other hand, is the seat of government, the commercial and banking centre of the country, and characteristically international. It possesses

good schools, excellent hospitals, many delightful houses, and an open-air theatre. It is expanding rapidly, and already five- and six-storey buildings are appearing. The University has grown greatly in the nine years since the present Visitor was last there, and the present buildings, especially those recently opened for the Medical School, together with the recent additions to the civil hospital nearby, impress one immensely as evidence of the spirit of progress. The hospital is well planned, well equipped, and efficiently run, and is the teaching hospital associated with the Medical School. The whole-time University clinical departments of Medicine, Surgery and Gynaecology have their beds there and, as in our own country, the part-time clinicians too play an important part in the teaching of students. There is a large volume and wonderful variety of clinical material and the investigation and treatment of patients is of high order. Moreover, improvements in laboratory services are constantly being introduced. For instance, during the past year a well-housed and well-organized blood bank has been established in the Hospital. Another recent addition is accommodation and X-ray apparatus for modern angiocardiography. Even more fundamental is the advance that educated Sudanese women are now entering the School of Nursing. But perhaps the most important is the appointment of two anaesthetists—one University and one Civil Hospital.

In all this stimulating environment it is not surprising, therefore, that teaching is good, and that specialists are working at the growing edge of their subjects. Indeed, it is right and proper that in the capital City and University Centre nothing but the highest standards should satisfy. Yet, within a few miles of the centre of Khartoum is open desert and, within ten, typical native villages and life of great simplicity. Apart from the Three Towns there are few of over 20,000 people anywhere, and during one's journeyings in the more distant parts of the country one realizes how utterly different from Khartoum are the circumstances under which medical practice is carried on, and that for the vast majority of the people the medical services will have to remain relatively simple until many more doctors are available. The problem is even greater when specialist work is concerned, and for many years to come the specialist who is something of a jack-of-all-trades will, excepting in the Capital, be of greater value than the purist. For instance, the surgeon who has had some training in fracture work, genito-urinary disease, the common abdominal conditions and, at the same time, can deal with a middle meningeal haemorrhage, or a haemopneumothorax due to trauma, will save more lives and restore to health more people than the most highly skilled purist. It should be remembered, too, that some forms of palliation such as ileostomy, or ileal bladder, would be insupportable for patients living in the bush: and treatment requiring constant supervision or frequent check-up offers nothing where communications are so poor. Fortunately, as

already said, the authorities are willing to transfer to Khartoum any patient requiring special treatment.

All this demands rather different and special training for the general duty officer and the specialist destined to work in the smaller Centres: indeed, under present circumstances it may well happen that the only doctor available to carry out some life-saving procedure on a patient too ill to be transferred to a larger Centre is a young man qualified only two or three years, and with only a year of resident postgraduate training.

For these various reasons it is heartening to see the Medical School and Hospital expanding and to know that the intake of new medical students next session is to be 40, and within a few years 50. It also explains why the Authorities hope very much indeed that until such time as more Sudanese specialists have become available, young specialists from Great Britain of Lecturer (clinical) or Senior Registrar grade will be willing to come to the Sudan for two or three years to help in the abundance of work that awaits more skill than is at present at hand; it would be an exciting and rewarding experience, and a strong preference for the British is repeatedly expressed.

AWAY FROM KHARTOUM

The Gezira

Whilst travelling around one could not help sensing the spirit of progress everywhere. In the Gezira, for instance, the irrigation scheme is being doubled and it is hoped soon to have 1,000,000 acres available for cotton, the main source of income for the whole country. The population of the Gezira is about 500,000. Something around 30,000 are tenants in the Government cotton scheme and during the picking season about 200,000 more receive temporary employment. With this further development the authorities plan new villages for the growing population, with wells, trees, street lighting and new schools.

En route for Wad Medani we called in on the Health Centre at Hassa Heisa with its impressively efficient midwifery and infant welfare services. Wad Medani itself, a town of 35,000 people, has a good hospital of 670 beds and with plans to increase by another 400. There are specialists in each of Medicine, Surgery and Gynaecology, and also centred there is a W.H.O. Tuberculosis Unit, with a records office, laboratory with a well-trained technician, and an X-ray Department with modern apparatus, including tomography and projection equipment. Its staff has beds for treatment up to several months, but their chief work is in visiting the homes in order to trace all contacts and to urge appropriate disposal and treatment.

Further south is the Sennar dam, which is at present being modified to give hydro-electric power, and it is hoped that this will be functioning within twelve months. Sennar has a hospital of 400 beds, rather simpler

in design than that at Wad Medani, but having its own surgeon and gynaecologist. Attached to it is a W.H.O. malaria unit, and again I was impressed by the keenness and intelligence of the Sudanese laboratory technician.

One unfortunate repercussion of irrigation is that the incidence of bilharzia has increased. Everywhere one sees preventive devices employed, such as screening, copper sulphate bags, or notices forbidding the public to bathe in the canals.

In all hospitals, health centres, dispensaries, etc., I saw a great variety of cases including many hernias, fractures, lacerations, burns (from bush fires), tuberculosis, bilharzia, malaria, madura, anaemias, kwashiorkor, leprosy, and a fascinating case of unilateral exophthalmos.

Equatoria

Equatoria is utterly different. Instead of open desert there are hills and trees and dried-up river beds which, during the rains, become absolute torrents. The ethnic groups are numerous and quite different from the northerners, there being many primitive tribes, so that language problems are great. All this adds to the difficulties of medical organization, and the value of a medical assistant is often commensurate with his knowledge of the predominant tribal language of the area served by his dispensary.

Dr. Osman Ibrahim very kindly acted as our guide and gave us much of his valuable time. He is just taking over from Dr. Abbas Hamed Nasr, who is moving to Kassala and was away when we first arrived. He introduced us both to the doctors and nursing staff of the Juba Hospital of 400 beds, with annexes for infectious cases (there was one of tetanus recovering).

THE MEDICAL SCHOOL

(*Dean: Professor H. Butler, M.A., M.D., B.Chir.*)

The new three-storey building mentioned in last year's report is now available and, in part, occupied. Being adjacent to the original Kitchener (now University) Medical School, and next door to the Stack laboratories and the civil hospital, the School-Hospital organization is ideally concentrated on one campus and augurs well for the future. It is an excellent building, giving generous floor space to all departments, allowing for lecture rooms, laboratories, demonstration rooms, seminar rooms, professors' and lecturers' rooms, preparation rooms and animal accommodation. There is no doubt that the School will possess as good amenities as can be found anywhere, and will comfortably and adequately accommodate the intake of 40 new students next October, rising to 50 without overcrowding. There are new separate departments of Medical Biochemistry and Bacteriology, and separate examinations in these subjects were held this year for the first time.

The strength of a Medical School depends, in part, upon the variety of interests of its members: its character, to a large extent, upon its students. In both respects this School is fortunate, and I was most especially impressed by the students, whose maturity and balance may well be in part because they live in University hostels. Their Medical Society asked me to give an evening lecture, and this gave me my first opportunity of meeting them. The lecture theatre was full, a number of questions were asked, and their President, in thanking me, presented me with all the issues of the first three years of their medical magazine, *El Hakeim*. This publication is of high order and contained many first-class articles. During the examinations a most pleasant and happy occasion took place when the students invited all the external examiners to take tea with them. This was held on the lawn of one of their hostels, and the invitation included those wives who happened to be in Khartoum. The Vice-Chancellor, Dean of the Faculty, Minister of Health, the Director of Medical Services, the Director of the Civil Hospital, together with many others of the medical fraternity, were also there and, indeed, were delighting in recalling their own happy student days in the same hostel. The students made charming hosts and impressed one with their intelligence and poise, yet with a delightful sense of humour. The more one met the young Sudanese the more one realized that once given the opportunity of contact with an advancing level of education, they are capable of taking full advantage of it, and of attaining the highest standard in professional and intellectual activities. The importance of the development of secondary schools is fully appreciated, since it is they who feed the University, and it was a great privilege to be taken round the fine Hantub School, near Wad Medani, which this year has 570 boys. My wife was also shown the Girls' Secondary School in Omdurman, which is doing excellent work and demonstrates the official policy of educating girls. Unfortunately, teachers cannot be manufactured overnight, which probably accounts for the fact that these schools aspire only to the equivalent of G.C.E. " O " level, and this at the age of 18 or 19 years. However, it has to be remembered that teaching is in English and that this " foreign " language has to be learned first—no mean task. This means that the course equivalent to first M.B. (" A " level) has to be taken at the University. This education is paid for by the Government, even though it has to be of necessity in boarding schools, and a small contribution is asked for where possible to cover the cost of residence. The cost of University education is also borne by the Government.

On referring to the full list of staff of the various University Departments it will be seen that there is a mixture of British and other expatriates on the one hand, and Sudanese on the other, and that the Sudanese are increasing in number. This is highly satisfactory and a pattern of the future.

DEPARTMENT OF SURGERY

In view of Julian Taylor's death earlier this year, a few words about his department seem appropriate. It seemed to me that it was a closely knit group of a highly skilled and progressive people under the leadership of one for whom all held the greatest respect and affection. Professor Taylor gave to his juniors every encouragement and practical support, and one suspects that many of the improvements in hospital services already reported are, in no small measure, due to his influence, and the recent appointment of two anaesthetic specialists is a major advance. His two ardent supporters, D. J. Crocket as Senior Lecturer, and J. E. Jacques as Lecturer, take their full share of general surgery, but have, respectively, fully established their two specialities, plastic surgery and thoracic surgery, including heart surgery, and excellent results are being obtained, whilst the Professor himself, with all his past experience and skill in the widest sense, applied the techniques of neurosurgery where needed. Mr. H. H. Barst, part-time surgeon at Omdurman, does much teaching during the long vacation, and Mr. Abdel Hamid Bayoumi, Senior Surgeon, teaches Surgical Anatomy.

The variety of disease is great and, again, includes many tropical diseases, especially maduramycosis, bilharzia and the tropical pattern of tuberculosis, as well as the commoner conditions as seen in Great Britain. It is interesting that peptic ulcer is becoming more common. The Department is especially interested in madura disease, and is trying new lines of treatment.

Professor Taylor, throughout his whole professional career, took especial interest in young men of promise who showed an enthusiasm for surgery. He did so at his own hospital, University College Hospital in London, and he repeated it in Khartoum. Of course, other Departments also have encouraged young Sudanese, but he seemed to be particularly successful in persuading these bright young men to prepare for the higher qualification of F.R.C.S. (England) by reading for the Primary F.R.C.S. Examination, and no less than 12 have already been successful. This results from the enthusiastic co-operation of all the preclinical departments, and Professor Taylor persuaded the Royal College of Surgeons of England to hold this Examination in Khartoum, which it has done twice. It is not surprising, therefore, that in almost every hospital in the Sudan one finds grateful and devoted young men determined to serve their country by qualifying as fully trained practical surgeons.

EXAMINERS' MEETING

The Vice-Chancellor thanked the examiners for their work and it was my privilege to reply. I said that I considered that the examinations had been run in an exemplary manner, and that I had found the performance of the candidates impressive and, indeed, in a few instances, outstanding.

This was evidence of good teaching as well as of the careful and successful selection of students, and it gave me great pleasure to repeat in public what I had expressed in private conversations, namely, that they offered a most promising potential for the future of medical man-power in all its facets for the Republic of the Sudan. As a result of the examinations the Sudan is richer by 22 doctors.

PERSONAL THANKS

My task as Visitor has been a most pleasant and memorable one, made so by universal friendliness, help and hospitality. The invitation came through the Vice-Chancellor of the University of Khartoum and the programme was arranged by the Minister of Health and the Director and Deputy Director of Medical Services, together with Professor Butler, the Dean. All members of the Medical School were most kind in showing me their departments and introducing me to their various colleagues. To these, and many more, we express our gratitude. Finally, once again, I should like to thank Dr. Hussein, P.M.O.H., and Dr. Gobani for their great kindness during our visit to the Gezira; and Dr. Abbas Hamed Nasr, P.M.O.H., and Dr. Osman Ibrahim, who is just succeeding him, for all they did for us whilst we were in Equatoria, centred on Juba.

INTERNATIONAL FEDERATION OF SURGICAL COLLEGES

THE INTERNATIONAL FEDERATION OF SURGICAL COLLEGES held its fourth Annual Meeting in Oslo on 12th, 13th and 14th September 1961. Excellent arrangements were made by the Norwegian Surgical Association, and the meetings were held in the house of the Norwegian Medical Association and in the University of Oslo.

Twenty different member-colleges were represented, and new members admitted were the Argentine Surgical Association, Association of Surgeons of East Africa, Israel Surgical Society and Spanish Association of Surgeons.

Sir Harry Platt, Bt. (U.K.), was re-elected President and Mr. Kennedy Cassels (U.K.) was re-elected Secretary and Treasurer, each for the ensuing three years. Professor Carl Semb (Norway) and Professor J.-L. Lortat-Jacob (France) were re-elected members of the Executive Committee.

It was decided to hold the next meeting in Atlantic City, U.S.A., on 13th and 14th October 1962, immediately before the Clinical Congress of the American College of Surgeons, when the topic for discussion will be the Interchange of Young Surgeons for purposes of training and research.

Later meetings were provisionally arranged for Rome in 1963 and Paris in 1964.

It was decided to stimulate member-colleges to set up in their own countries committees designed to collaborate with the national Red Cross Society in recruiting emergency surgical teams when necessary. Arrangements were also confirmed for periodical meetings between the International Federation and the World Health Organization and the League of Red Cross Societies for discussion of matters of common concern.

The Council received reports from its four Working Parties on the Training of Surgeons, Surgical Research, Surgical Missions, and Interchange of Young Surgeons. The following resolutions, among others, were passed:

(i) That, in the education and training of the young surgeon, due attention should be paid to the importance of experience in the organisation, scope and techniques of the auxiliary services, for example:
   (*a*) Resuscitation and blood transfusion;
   (*b*) Rehabilitation;
   (*c*) Laboratory and radiological diagnoses;
   (*d*) Nursing.

(ii) That research on surgery and chemotherapy as a combined therapy against malignant diseases should be further encouraged by members of the Federation.

(iii) That the attention of the World Health Organization be drawn to the importance of the universal problem of infection in hospitals and that W.H.O. be asked to support research programmes pertaining to the aetiology and prevention of hospital infections.

(iv) That research on mass casualties from irradiation should be handled on a national rather than an international basis, and that research on long-term storage of whole blood or plasma, or the development of better plasma substitutes, should be encouraged.

(v) That the International Federation should encourage the interchange of young surgeons between the countries represented in the Federation, believing that the most important function of the Federation is to improve surgical standards.

An Open Discussion was held on the topic " How can the International Federation foster surgical research on an international basis?", the principal speakers being Professor I. S. Ravdin (U.S.A.) and Professor Digby Chamberlain (U.K.).

The remainder of the meeting (nearly three half-days) was occupied in reading short communications on recent research work. In the first part of the programme the subjects were those selected by the International Federation for study on an international basis, namely Malignant Disease; Infection in Wounds; the Transplantation of Tissues and Organs; and Mass Casualties from Irradiation and Other Accidents. Each of these topics was opened by an American surgeon, and the papers which followed were read by surgeons from Norway, Denmark, Sweden and Finland. The second programme was contributed entirely by Scandinavians, and the topics were varied. It was generally agreed that the papers reached a high standard, and it is hoped to publish abstracts from them at a later date.

At the end of the meeting a very interesting demonstration was given by a Norwegian military unit, showing the landing of a surgical relief team by helicopter, reinforcement by an infantry unit from the ground, and the grading of casualties into their appropriate priorities for treatment. A running commentary in English was given by Norwegian medical officers.

A dinner was held at the Continental Hotel at which the company (97 in number) were welcomed by Dr. Gudmund Semb, local secretary of the meeting, and the speakers were Professor Christian Brüüsgaard, President of the Norwegian Surgical Society, and Sir Harry Platt, Bt., President of the International Federation of Surgical Colleges.

PRIMARY FELLOWSHIP EXAMINATIONS OVERSEAS

THE COUNCIL HAS agreed to requests from the Government of Pakistan, the University of Ceylon and the University of Khartoum, for Primary Fellowship Examinations to be held as follows in 1962:

January 1962	Primary F.R.C.S. Examinations in Lahore and Colombo.
	Primary F.D.S.R.C.S. Examination in Colombo.
March 1962	Primary F.R.C.S. Examination in Khartoum.

Examiners appointed so far include Professor Digby Chamberlain, Vice-President, Sir Cecil Wakeley, Bt., Professor R. Milnes Walker, Professor Robert Knox, Professor D. Slome and Professor R. J. Last to examine in Lahore; Professor Chamberlain, Professor Milnes Walker, Professor Last and Professor Martin Ruston, Dean of the Faculty of Dental Surgery, to examine in Ceylon; and Professor Chamberlain, Professor Charles Wells, Mr. T. Holmes Sellors, and Professor G. H. Bell to examine in Khartoum. In addition, Professor A. C. E. Koch, Professor Milroy Paul and Professor G. H. Cooray will take part in the examinations in Ceylon; and Professor H. A. Butler, Dean of the Faculty of Medicine, will examine in Khartoum.

The examinations in Lahore will be the first to be held in Pakistan; although a request was made for one to be held there in 1950 this was cancelled on account of the lack of sufficient candidates. It is expected that, in January, there will be between thirty and fifty candidates from Pakistan, and Professor R. J. Last has recently returned from Lahore where he supervised a preparatory course in the basic medical sciences.

PROCEEDINGS OF THE COUNCIL IN OCTOBER

AT A MEETING of the Council on 12th October 1961, with Sir Arthur Porritt, President, in the Chair, a resolution of condolence was passed on the death of Professor Lambert Charles Rogers, C.B.E., V.R.D., F.R.C.S., a past member of Council and Court of Examiners and Vice-President.

The death of Professor Raffaele Bastianelli of Rome (Honorary Fellow) was recorded with deep regret.

The admission of Mr. F. R. Moser to the Honorary Fellowship in the Faculty of Dental Surgery was reported.

The Hallett Prize was presented to Miss I. Sri Skanda Rajah of the University of Ceylon, to whom it had been awarded at the Primary Fellowship Examination in Ceylon in January 1960.

Handcock Prizes were presented to Miss J. B. Brown of St. Thomas's Hospital Medical School and Dr. N. K. Coni of Westminster Medical School.

Long service awards and McNeill Love Medals were presented to three members of the College Staff—Mr. S. Wood (60 years' service), Mr. S. P. Steward (49 years' service), and Mr. J. C. Higgins (44 years' service).

The first F. R. Moser Prize of £500 for distinction in dental research was awarded to Professor A. I. Darling, F.D.S.R.C.S., of the University of Bristol.

Mr. J. B. Oldham, F.R.C.S., was re-appointed as representative of the College on the Court of the University of Liverpool.

Diplomas of Fellowship were granted to M. A. Ilahi and T. Coetzee.

A Diploma of Fellowship in Dental Surgery was granted to B. C. O'Riordan.

Diplomas of Fellowship in the Faculty of Anaesthetists were granted to M. Evans and J. D. Hill as from 3rd August 1961.

Three Diplomas of Membership and eight Diplomas in Orthodontics were granted.

The following diplomas were granted, jointly with the Royal College of Physicians: *Ophthalmology* (47), *Laryngology and Otology* (2), *Child Health* (102), *Physical Medicine* (5), *Tropical Medicine and Hygiene* (53).

Professor G. J. Cunningham was appointed as External Examiner at the next Primary Fellowship Examination of the Royal Faculty of Physicians and Surgeons of Glasgow.

Examiners were appointed for the Primary Fellowship examination to be held in Khartoum in March 1962.

The following hospitals were recognized under paragraph 23 of the Fellowship regulations:

Hospitals	Posts Recognized		
	General (6 months unless otherwise stated)	Casualty (all 6 months)	Unspecified (all 6 months)
Swindon—Princess Margaret and Victoria Hospitals (additional)			*Under para.* 23 (*b*) Resident H.O. (Ophth.)
Ascot—Heatherwood Hospital (additional)		Cas. S.H.O.	
Salisbury—General Hospital (decennial and additional)	R.S.O. (Regr.) 3 H.Ss.	Cas. Offr.	2 Orth. Regrs. 1 Regr. (Plastic) 2 S.H.Os. (Plastic)
Romford—Oldchurch Hospital (additional)			*Under para.* 23 (*b*) Regr. Ophth. (12m) S.H.O. Ophth. (6m)
London—Neasden Hospital			*Under para.* 23 (*b*) Regr. Ophth. (12m)
Preston—Royal Infirmary (additional)			*Under para.* 23 (*b*) Regr. (Ophth.)
Oldham and District General Hospital (redesignation)			*Under para.* 23 (*c*) S.H.O. now redesignated Regr.
London—Highlands General Hospital (redesignation)			H.S. (Orth.) now redesignated S.H.O. (Orth.)
New Zealand—Timaru Hospital	H.S.	Cas. Offr.	
India—Neyyoor, Kaniyakumari Medical Mission (additional)	Regr.	Cas. Offr.	

INCREASE IN SUBSCRIPTION RATE

The Editor regrets that, owing to the recent rise in printing costs, it has been found necessary to increase the rate of subscription to the *Annals* to £3 0s. 0d. p.a., post free. This increase will take effect from July 1962 and new Banker's Order forms will be circulated in a future issue of the *Annals*.

ANATOMICAL MUSEUM

THE SPECIAL DISPLAYS are discontinued temporarily as the third floor museum is being used for other purposes.

DIARY FOR NOVEMBER

Fri.	17	5.00	Board of Faculty of Dental Surgery.
Tues.	21		First L.D.S. Examination begins.
		5.00	DR. R. C. B. PUGH—Erasmus Wilson Demonstration—Histopathology of the prostate.
		5.00	PROFESSOR L. P. GARROD—Dental Lecture—Antibiotic therapy.
		6.15	DR. S. BLACKMAN—Dental Lecture—Radiology of the jaws—I.
Thurs.	23	5.00	PROFESSOR R. B. LUCAS—Dental Lecture—Clinical pathology.
		6.15	DR. S. BLACKMAN—Dental Lecture—Radiology of the jaws—II.
Fri.	24	7.30	Dinner of Fellows and Members—Sheffield.
Sat.	25	2.15	Annual Meeting of Fellows and Members—Sheffield.
		3.00	SIR HOWARD FLOREY, P.R.S.—The Arthur Hall Lecture in Sheffield—Electron microscopy and surgery.
Mon.	27		D.L.O. Examination (Part I) begins.
Tues.	28		Second L.D.S. Examination begins.
		5.00	PROFESSOR A. I. DARLING—Dental Lecture—Dental caries—I.
		6.15	PROFESSOR A. I. DARLING—Dental Lecture—Dental caries—II.
Thurs.	30	5.00	PROFESSOR G. L. HOWE—Dental Lecture—Oral surgery in relation to prosthetic problems.
		5.30	PROFESSOR F. BERGEL, F.R.S.—Otolaryngology Lecture—The newer developments in carcino-chemotherapy.
		6.15	MR. B. W. FICKLING—Dental Lecture—The maxillary antrum in relation to dental surgery.

DIARY FOR DECEMBER

Fri.	1		Date of election of Fellows to the Board of Anaesthetists announced.
Mon.	4		First Membership Examination and D.P.H. Examination begin.
Tues.	5		D.L.O. Examination (Part II) begins.
Thurs.	7	5.00	PROFESSOR J. B. M. ROBERTS—Hunterian Lecture—Spina bifida of the urinary tract.
Mon.	11	5.00	SIR WILFRED LE GROS CLARK—Edridge Green Lecture—The sorting principle in sensory analysis as illustrated by the visual pathways.
Wed.	13	5.00	DR. I. FRIEDMANN—Erasmus Wilson Demonstration—Electron microscopy.
Thurs.	14	2.00	Ordinary Council.
		5.00	MR. WILLIAM GISSANE—Robert Jones Lecture—The basic surgery of major injuries of the motorways.
Fri.	15		Dental Lectures and Clinical Conferences end.
Wed.	20	5.00	Board of Faculty of Anaesthetists.
Sat.	23		College closed.
Mon.	25		College closed.
Tues.	26		College closed.
Wed.	27		College closed.

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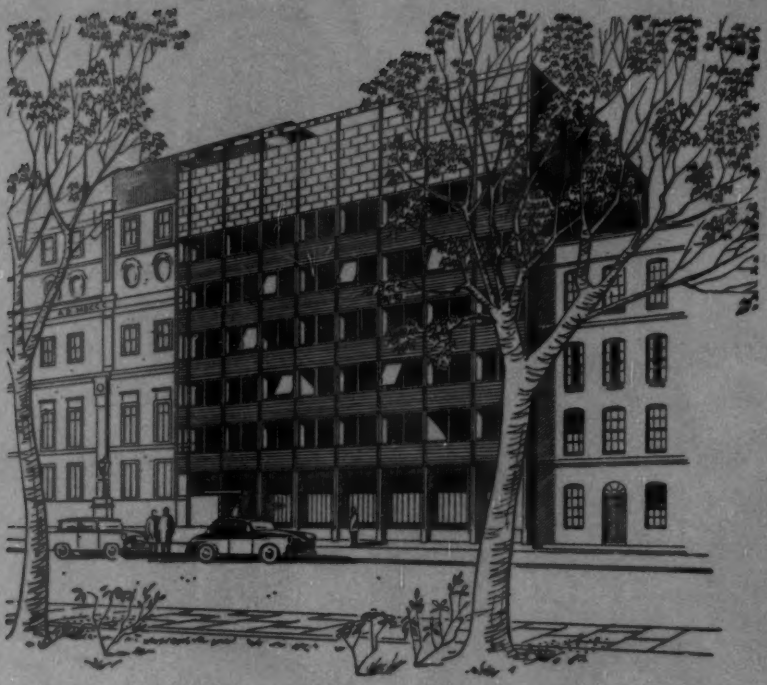

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